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21 August 1959

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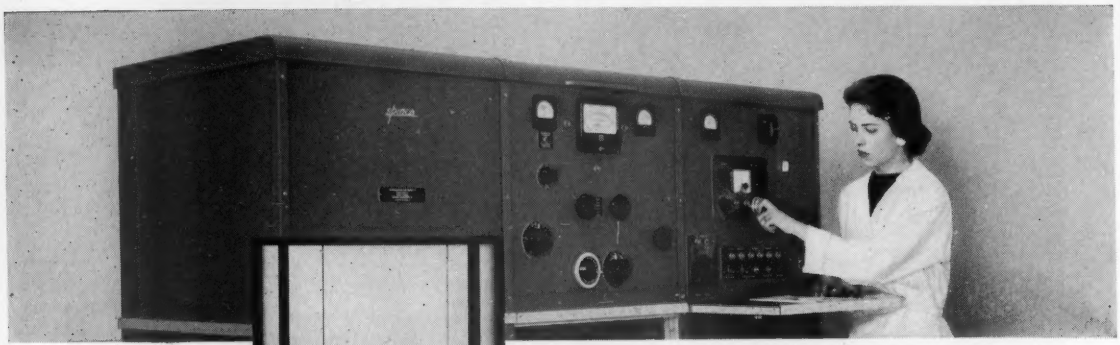
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

New Methods Extend the Usefulness of the Ultracentrifuge

Recent studies by research scientists have further increased the uses of the Analytical Ultracentrifuge for measuring molecular weights and purity of viruses, enzymes, proteins, polymers and a variety of organic and inorganic molecules. Here are four new developments as reported in the technical literature.



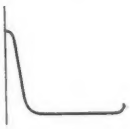
Interacting Systems

Kegeles and Rao at Clark University have measured the molecular weights of chemically reacting systems in the ultracentrifuge cell using the Archibald "approach-to-equilibrium" method. Studying the enzyme system alpha-chymotrypsin, they showed it to be present in the ultracentrifuge cell as an equilibrium mixture of monomers, dimers, and trimers. This is an extension of previous work which showed that the Archibald method applies to polydisperse non-ideal solutions, as well as to monodisperse ideal solutions.

Improved Accuracy

Trautman, at New York's Rockefeller Institute for Medical Research, showed that the accuracy of the Archibald method can be improved by more precisely locating the position of the meniscus on the ultracentrifuge photographic plate. He made a detailed study of the optical fine structure at the meniscus, and used a special optical aligning procedure with a mirror in the ultracentrifuge cell.

Simplified Measurements



At Stockholm's Nobel Medical Institute, Ehrenberg reports a simplified approach-to-equilibrium method which makes measurements from the schlieren curve easier. He runs the ultracentrifuge fast enough for a peak to begin forming at the meniscus so that the schlieren curve is parallel with the baseline and no extrapolation is necessary. His measurements of molecular weight and diffusion constants agree closely with those by other methods.

Rapid Equilibrium

Van Holde and Baldwin at the University of Wisconsin have used short liquid columns to achieve complete sedimentation equilibrium in a fraction of the time previously required. Using liquid columns of only 3 mm, they report equilibrium with sucrose in 3½ hours, and with a 1 mm column in only 30 minutes. In addition, the authors report that measurements during approach-to-equilibrium permit calculation of a diffusion coefficient.

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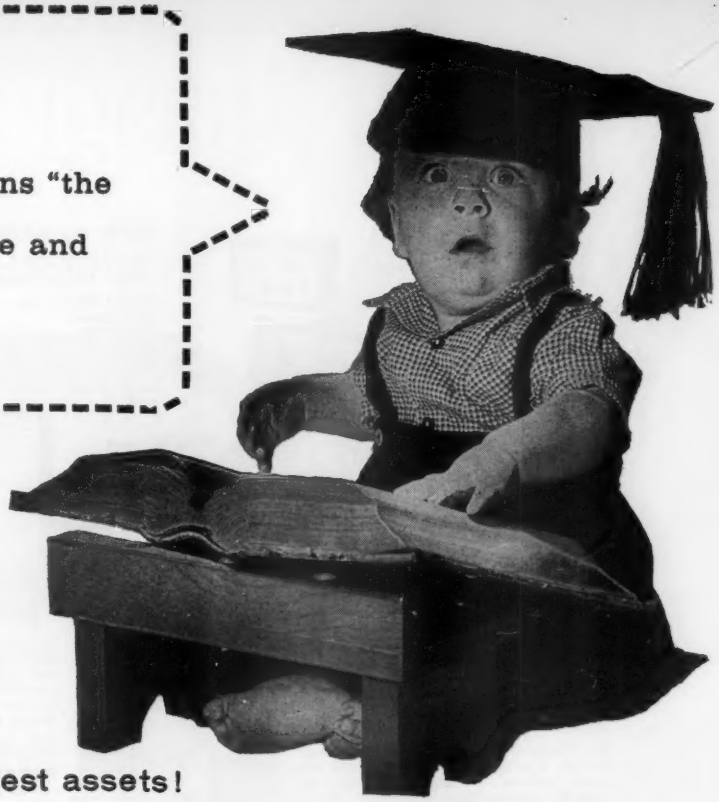

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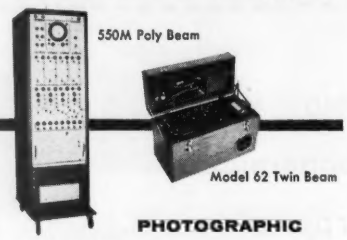

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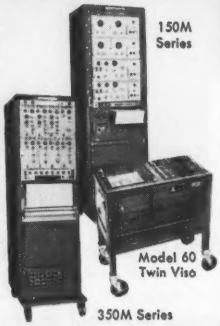

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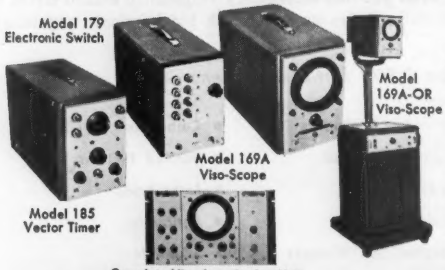

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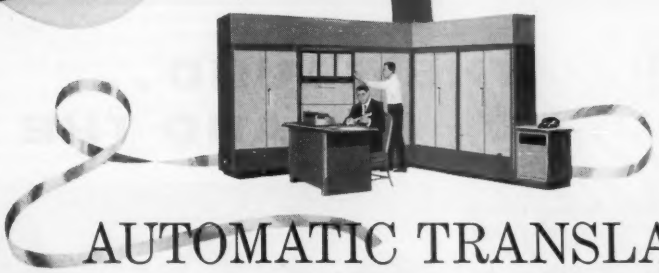

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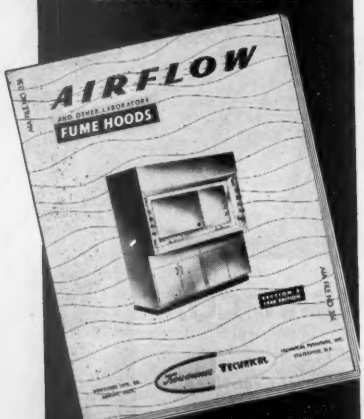

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Letters

Peking Man

In the "News of science" section of *Science* [**129**, 825 (1959)] you ask, "Where is Peking Man?" and speculate on some of the possible answers to this question. As a former member of the American Embassy guard at Peking, China, at the outbreak of World War II, I would like to rule out the theory that the Peking Man may be at the bottom of the Yangtze River.

The S.S. *Harrison* had just taken the 4th Marines from Shanghai to the Philippine Islands and was returning to China for those of us who were still in North China. The war caught the ship just off the coast of China near Shanghai, and the captain ran it aground. This was hundreds of miles from Chinwangtao, and thus the Peking Man never went aboard the *Harrison*.

I recall seeing some cases in Peking marked for Johns Hopkins University and believe these contained the collection. If so, I am fairly certain they arrived safely in Chinwangtao.

Since we were preparing to leave China on Thursday, 11 Dec. 1941, we had packed up all our guns, ammunition, and other equipment and had sent it to Chinwangtao. Because of the facilities in that small Marine outpost, it is quite likely that the Peking Man was stored with our things.

When the war broke out, the approximately 35 men stationed in Chinwangtao were moved to Tientsin, and we were moved from Peking to Tientsin.

It may be that the Peking Man was discarded as unimportant in the looting of our supplies—that it was thrown out with the usual debris of such lootings. If this was the case, there is a good chance that the collection is still in the vicinity of the camp at Chinwangtao or that it fell into the hands of the Chinese and was used for medicine, as was the practice.

The nature of the packing, however, would indicate to the looters that the contents were of some value, and, for this reason, I doubt very much if the collection was thrown out.

Since the Japanese at the time had a great need for military supplies and since our equipment was all packed and ready to go, it may be that the Peking Man was shipped out with our equipment to some point within the Japanese war theater. If this is the case, the collection could still be in existence in any one of a number of places, from the Aleutians to Borneo.

It seems that a check with Japanese Army records, to locate the soldiers who were stationed at Chinwangtao, would be a logical step in trying to locate the collection. Perhaps the men who were there could tell what happened to it.

One thing is certain: the Peking Man was not on the S.S. *Harrison*.

GERALD L. BEEMAN
Cleveland Museum of Natural History, Cleveland, Ohio

Nuclear Research

There are several errors in the editorial entitled "Capital gain" [*Science* **129**, 1583 (1959)]. The most important one, and the only one I will point out here, is the position stated in the editorial that, due to "special security requirements," the Department of Defense should have no more than (and by implication, less than) a modest share in nuclear research. As the decision to place the Stanford accelerator under the AEC is applauded on this basis, it is further implied that the AEC has no similar "special security requirements."

I challenge the writer of the editorial to visit the following accelerator facilities operating under Navy contract: the Mark III at Stanford, the 450-Mev proton synchrocyclotron at Chicago, the 400-Mev proton synchrocyclotron at Columbia, the 1.5-Bev electron synchrotron at Cornell—or any nuclear physics facility operating under Office of Naval Research contract. I would then like to have him visit Argonne, Brookhaven, the Radiation Laboratory, and other AEC accelerator facilities and make an *honest* report comparing the "special security requirements" of the Department of Defense and the AEC. (He might also be interested in finding out why Fermi chose Navy support for the Chicago accelerator instead of AEC support.)

If he is concerned with the "special security requirements" of the Department of Defense as a whole, then he should be equally concerned with the "special security requirements" of the AEC as a whole. He should also be lamenting the assignment of the Stanford project to the AEC, instead of the National Science Foundation, for example, due to the AEC's "special security requirements" and, more important yet, due to the strengthening of the AEC monopoly on high-energy accelerator physics. This assignment is in direct opposition to the report's strong recommendation of diversity of support—there must have been reason for such a recommendation.

It might also interest the writer of the editorial to find out who kept the Stanford proposal alive and provided the major drive to see that it was finally approved.

ALBERT G. OPITZ
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—*Opticks*, 1704

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Two Cultures

We are living in the middle of two cultures which have scarcely any contact at all—the traditional non-scientific culture and an up-and-coming scientific one. They are startlingly different, but only in their intellectual approach, but even more so in their climate of thought and their moral attitudes. This divide exists not only in the U.S. and Great Britain but all over the Western world. I happen to have been forced to notice it because, through a set of chances, I have spent a good deal of my working life sitting with scientists in the afternoon, as it were, and talking to writers at night. Just how this happened doesn't matter except to me; but perhaps I might mention that, though I knew my vocation as a novelist before I was twenty, I was trained as a scientist and did some research at Cambridge. . . . After that I got involved in science-and-government, and through these various chances I could not very well avoid seeing more than most people of the two sides of the cultural divide. And I have become increasingly worried by what I have seen. . . .

What can we do about it? There is only one answer, and it is a prosaic one: sensible education. Nearly all intelligent people can learn something about science and scientists if they are brought up against them properly. It is very stupid to attempt to make everybody into technologists; but it is essential that everybody, including the technologists themselves, should understand something of the intellectual and human meaning of what the technologists are about. I don't think that that task is beyond us, though it will need a drastic rethinking about education, both in the U.S. and Great Britain.

There is just one basic difficulty. All children have a dash of the scientist in them. Watch any bright child if you tell him about the stars or atoms or dinosaurs. He will want to find out some more. The urge to investigate, which is the scientific urge, isn't anything very special or academic. It is one of the most human things about us. In that sense, as I said, all children are scientists. But all children are not mathematicians, and that is the core of the difficulty. I don't know how many people are mathematically blind to the extent that some of us are tone deaf, but I suspect a larger proportion than the educational psychologists usually allow. Thinking of twenty acquaintances, who have all done pretty well in various sorts of intellectual life, I should say that at least five were, if not mathematically blind, at least grossly deficient in mathematical sense. That means that though, sensibly educated, they could have got a good working idea of how physical science goes about its business, they would never have reached the fundamental concepts. I suggest we have got to accept the fact that, for a lot of people of high intelligence and imagination, this is as near as they are going to come to the real stuff. It is much better than nothing, but there are limits, and it is just as well to be clear-sighted about them in advance.

Don't we know enough now of the way different kinds of intelligence work? Oughtn't we to be able to construct an education from which anyone of ability can get enough not to feel that the scientific experience is alien to him forever?—C. P. SNOW. [From the prefatory note to *The Search* by C. P. Snow, copyright 1934, 1958, by Charles Percy Snow. Reprinted with the permission of Charles Scribner's Sons.]

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CURRENT PROBLEMS IN RESEARCH

Affectional Responses in the Infant Monkey

Orphaned baby monkeys develop a strong and persistent attachment to inanimate surrogate mothers.

Harry F. Harlow and Robert R. Zimmermann

Investigators from diverse behavioral fields have long recognized the strong attachment of the neonatal and infantile animal to its mother. Although this affectional behavior has been commonly observed, there is, outside the field of ethology, scant experimental evidence permitting identification of the factors critical to the formation of this bond. Lorenz (*1*) and others have stressed the importance of innate visual and auditory mechanisms which, through the process of imprinting, give rise to persisting following responses in the infant bird and fish. Imprinting behavior has been demonstrated successfully in a variety of avian species under controlled laboratory conditions, and this phenomenon has been investigated systematically in order to identify those variables which contribute to its development and maintenance [see, for example, Hinde, Thorpe, and Vince (*2*), Fabricius (*3*), Hess (*4*), Jaynes (*5*), and Moltz and Rosenblum (*6*)]. These studies represent the largest body of existent experimental evidence measuring the tie between infant and mother. At the mammalian level there is little or no systematic experimental evidence of this nature.

Observations on monkeys by Carpenter (*7*), Nolte (*8*), and Zuckermann (*9*) and on chimpanzees by Kohler (*10*) and by Yerkes and Tomilin (*11*) show that monkey and chimpanzee infants develop strong ties to their mothers and that these affectional attachments may persist for years. It is, of course, common knowledge that human infants form strong and persistent ties to their mothers.

Although students from diverse scientific fields recognize this abiding attachment, there is considerable disagreement about the nature of its development and its fundamental underlying mechanisms. A common theory among psychologists, sociologists, and anthropologists is that of learning based on drive reduction. This theory proposes that the infant's attachment to the mother results from the association of the mother's face and form with the alleviation of certain primary drive states, particularly hunger and thirst. Thus, through learning, affection becomes a self-supporting, derived drive (*12*). Psychoanalysts, on the other hand, have stressed the importance of various innate needs, such as a need to suck and orally possess the breast (*2*), or needs relating to contact, movement, temperature (*13*), and clinging to the mother (*14*).

The paucity of experimental evidence concerning the development of affectional responses has led these theorists to derive their basic hypotheses from deductions and intuitions based on observation and analysis of adult verbal reports. As a result, the available observational evidence is often forced into a preconceived theoretical framework. An exception to the above generalization is seen in the recent attempt by Bowlby (*14*) to analyze and integrate the available observational and experimental evidence derived from both human and subhuman infants. Bowlby has concluded that a theory of component instinctual responses, species specific, can best account for the infant's tie to the mother. He suggests that the species-specific responses for human beings (some of these responses are not strictly limited to human beings) include contact, clinging, sucking, crying, smiling, and following. He further emphasizes that these responses are manifested independently of primary drive reduction in human and subhuman infants.

The absence of experimental data which would allow a critical evaluation of any theory of affectional development can be attributed to several causes. The use of human infants as subjects has serious limitations, since it is not feasible to employ all the experimental controls which would permit a completely adequate analysis of the proposed variables. In addition, the limited response repertoire of the human neonate severely restricts the number of discrete or precise response categories that can be measured until a considerable age has been attained. Thus, critical variables go unmeasured and become lost or confounded among the complex physiological, psychological, and cultural factors which influence the developing human infant.

Moreover, the use of common laboratory animals also has serious limitations, for most of these animals have behavioral repertoires very different from those of the human being, and in many species these systems mature so rapidly that it is difficult to measure and assess their orderly development. On the other hand, subhuman primates, including the macaque monkey, are born at a state of maturity which makes it possible to begin precise measurements within the first few days of life. Furthermore, their postnatal maturational rate is slow enough to permit precise assessment of affectional variables and development.

Over a 3-year period prior to the beginning of the research program reported

The authors are on the staff of the primate laboratory, department of psychology, University of Wisconsin, Madison.

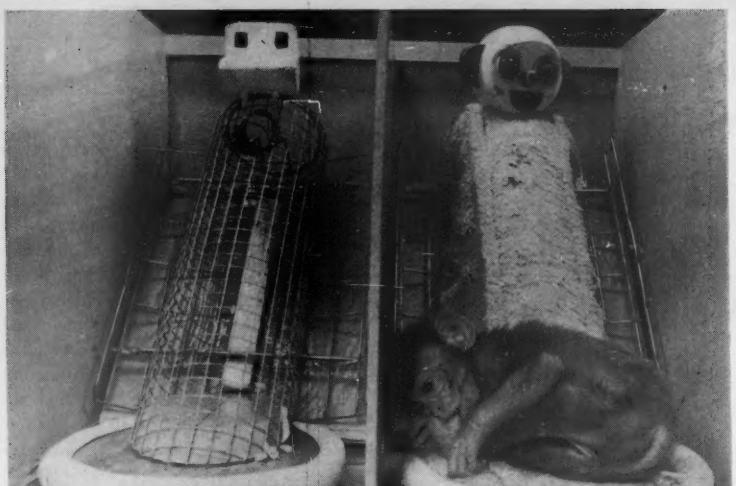


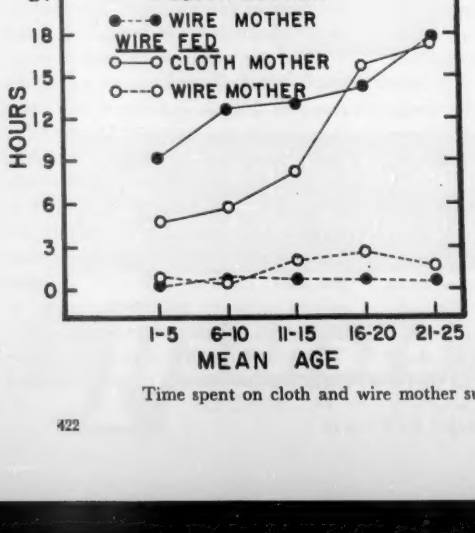
Fig. 1. Wire and cloth mother surrogates.

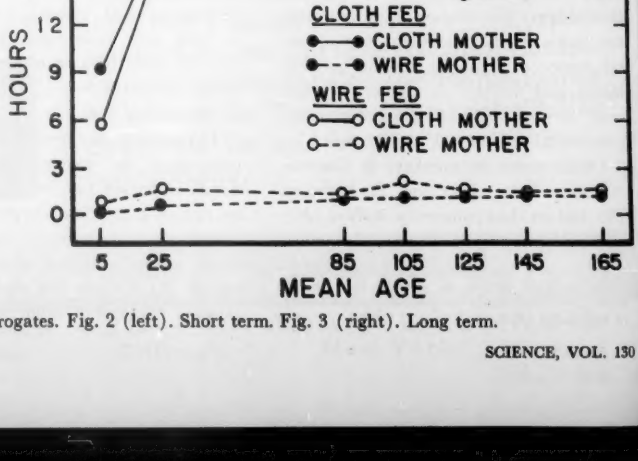
here (*15*), some 60 infant macaque monkeys were separated from their mothers 6 to 12 hours after birth and raised at the primate laboratory of the University of Wisconsin. The success of the procedures developed to care for these neonates was demonstrated by the low mortality and by a gain in weight which was approximately 25 percent greater than that of infants raised by their own mothers. All credit for the success of this program belongs to van Wagenen (*16*), who had described the essential procedures in detail.

These first 3 years were spent in devising measures to assess the multiple capabilities of the neonatal and infantile monkey. The studies which resulted have revealed that the development of perception, learning, manipulation, exploration, frustration, and timidity in the macaque monkey follows a course and sequence which is very similar to that in the human infant. The basic differences between the two species appear to be the advanced postnatal maturational status and the subsequent more rapid growth of the infant macaque. Probably the most important similarities between the two, in relation to the problem of affectional development, are characteristic responses that have been associated with, and are considered basic to, affection; these include nursing, clinging, and visual and auditory exploration.

In the course of raising these infants we observed that they all showed a strong attachment to the cheesecloth blankets which were used to cover the wire floors of their cages. Removal of these cloth blankets resulted in violent emotional behavior. These responses were not short-lived; indeed, the emotional disturbance lasted several days, as was indicated by the infant's refusal to work on the standard learning tests that were being conducted at the time. Similar observations had already been made by Foley (*17*) and by van Wagenen (*16*), who stressed the importance of adequate contact responses to the very survival of the neonatal macaque. Such observations suggested to us that contact was a true affectional variable and that it should be possible to trace and measure the development and importance of these responses. Indeed there seemed to be every reason to believe that one could manipulate all variables which have been considered critical to the development of the infant's attachment to a mother, or mother surrogate.

To attain control over maternal variables, we took the calculated risk of constructing and using inanimate mother surrogates rather than real mothers. The cloth mother that we used was a cylinder of wood covered with a sheath of terry cloth (*18*), and the wire mother was a hardware-cloth cylinder. Initially, sponge rubber was placed underneath the terry cloth sheath of the cloth mother surrogate, and a light bulb behind each mother surrogate provided radiant heat. For reasons of sanitation





Time spent on cloth and wire mother surrogates. Fig. 2 (left). Short term. Fig. 3 (right). Long term.

and safety these two factors were eliminated in construction of the standard mothers, with no observable effect on the behavior of the infants. The two mothers were attached at a 45-degree angle to aluminum bases and were given different faces to assure uniqueness in the various test situations (Fig. 1). Bottle holders were installed in the upper middle part of the bodies to permit nursing. The mother was designed on the basis of previous experience with infant monkeys, which suggested that nursing in an upright or inclined position with something for the infant to clasp facilitated successful nursing and resulted in healthier infants (see *16*). Thus, both mothers provided the basic known requirements for adequate nursing, but the cloth mother provided an additional variable of contact comfort. That both of these surrogate mothers provided adequate nursing support is shown by the fact that the total ingestion of formula and the weight gain was normal for all infants fed on the surrogate mothers. The only consistent difference between the groups lay in the softer stools of the infants fed on the wire mother.

Development of Affectional Responses

The initial experiments on the development of affectional responses have already been reported (*19*) but will be briefly reviewed here, since subsequent experiments were derived from them. In the initial experiments, designed to evaluate the role of nursing on the development of affection, a cloth mother and a wire mother were placed in different cubicles attached to the infant's living cage. Eight newborn monkeys were placed in individual cages with the surrogates; for four infant monkeys the cloth mother lactated and the wire mother did not, and for the other four this condition was reversed.

The infants lived with their mother surrogates for a minimum of 165 days, and during this time they were tested in a variety of situations designed to measure the development of affectional responsiveness. Differential affectional responsiveness was initially measured in terms of mean hours per day spent on the cloth and on the wire mothers under two conditions of feeding, as shown in Fig. 2. Infants fed on the cloth mother and on the wire mother have highly similar scores after a short adaptation period (Fig. 3), and over a 165-day period both groups show a distinct preference for the cloth mother. The persistence of the differential responsiveness to the mothers for both groups of infants is evident, and the over-all differences between the groups fall short of statistical significance.

Fig. 4. Typical fear stimulus.

These data make it obvious that contact comfort is a variable of critical importance in the development of affectional responsiveness to the surrogate mother, and that nursing appears to play a negligible role. With increasing age and opportunity to learn, an infant fed from a lactating wire mother does not become more responsive to her, as would be predicted from a derived-drive theory, but instead becomes increasingly more responsive to its nonlactating cloth mother. These findings are at complete variance with a drive-reduction theory of affectional development.

The amount of time spent on the mother does not necessarily indicate an affectional attachment. It could merely reflect the fact that the cloth mother is a more comfortable sleeping platform or a more adequate source of warmth for the infant. However, three of the four infants nursed by the cloth mother and one of the four nursed by the wire mother left a gauze-covered heating pad that was on the floor of their cages during the first 14 days of life to spend up to 18 hours a day on the cloth mother. This suggests that differential heating or warmth is not a critical variable within the controlled temperature range of the laboratory.

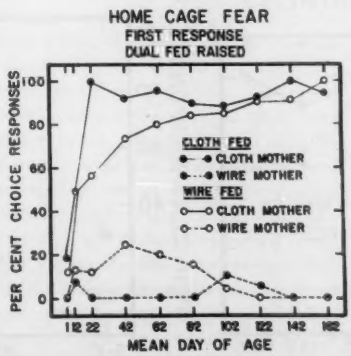


Fig. 5. Differential responsiveness in fear tests.

Other tests demonstrate that the cloth mother is more than a convenient nest; indeed, they show that a bond develops between infant and cloth-mother surrogate that is almost unbelievably similar to the bond established between human mother and child. One highly definitive test measured the selective maternal responsiveness of the monkey infants under conditions of distress or fear.

Various fear-producing stimuli, such as the moving toy bear illustrated in Fig. 4, were presented to the infants in their home cages. The data on differential responses under both feeding conditions are given in Fig. 5. It is apparent that the cloth mother was highly preferred to the wire mother, and it is a fact that these differences were unrelated to feeding conditions—that is, nursing on the cloth or on the wire mother. Above and beyond these objective data are observations on the form of the infants' responses in this situation. In spite of their abject terror, the infant monkeys, after reaching the cloth mother and rubbing their bodies about hers, rapidly come to lose their fear of the frightening stimuli. Indeed, within a minute or two most of the babies were visually exploring the very thing which so shortly before had seemed an object of evil. The bravest of the babies would actually leave the mother and approach the fearful monsters, under, of course, the protective gaze of their mothers.

These data are highly similar, in terms of differential responsiveness, to the time scores previously mentioned and indicate the overwhelming importance of contact comfort. The results are so striking as to suggest that the primary function of nursing may be that of insuring frequent and intimate contact between mother and infant, thus facilitating the localization of the source of contact comfort. This interpretation finds some support in the test discussed above. In both situations the infants

nursed by the cloth mother developed consistent responsiveness to the soft mother earlier in testing than did the infants nursed by the wire mother, and during this transient period the latter group was slightly more responsive to the wire mother than the former group. However, these early differences shortly disappeared.

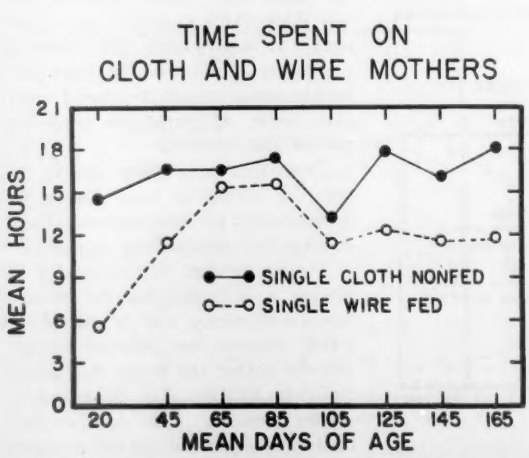
Additional data have been obtained from two groups of four monkeys each which were raised with a single mother placed in a cubicle attached to the living-cage. Four of the infants were presented with a lactating wire mother and the other four were presented with a nonlactating cloth mother. The latter group was hand-fed from small nursing bottles for the first 30 days of life and then weaned to a cup. The development of responsiveness to the mothers was studied for 165 days; after this the individual mothers were removed from the cages and testing was continued to determine the strength and persistence of the affectional responses.

Figure 6 presents the mean time per day spent on the respective mothers over the 165-day test period, and Fig. 7 shows the percentage of responses to the mothers when a fear-producing stimulus was introduced into the home cage. These tests indicate that both groups of infants developed responsiveness to their mother surrogates. However, these measures did not reveal the differences in behavior that were displayed in the reactions to the mothers when the fear stimuli were presented. The infants raised on the cloth mother would rush to the mother and cling tightly to her. Following this initial response these infants would relax and either begin to manipulate the mother or turn to gaze at the feared object without the slightest sign of apprehension. The infants raised on the wire mother, on the other hand, rushed away from the feared object toward their mother but did not cling to or embrace her. Instead, they would either clutch themselves and rock and vocalize for the remainder of the test or rub against the side of the cubicle. Contact with the cubicle or the mother did not reduce the emotionality produced by the introduction of the fear stimulus. These differences are revealed in emotionality scores, for behavior such as vocalization, crouching, rocking, and sucking, recorded during the test. Figure 8 shows the mean emotionality index for test sessions for the two experimental groups, the dual-mother groups, and a comparable control group raised under standard laboratory conditions. As can be seen, the infants raised with the single wire mother have the highest emotionality scores of all the groups, and the infants raised with the single cloth mother or with a cloth and wire mother have the lowest scores. It appears that the responses made by infants raised only with a wire mother were more in the nature of simple flight responses to the fear stimulus and that the presence of the mother surrogate had little effect in alleviating the fear.

During our initial experiments with the dual-mother conditions, responsiveness to the lactating wire mother in the fear tests decreased with age and opportunity to learn, while responsiveness to the nonlactating cloth mother increased. However, there was some indication of a slight increase in frequency of response to the wire mother for the first 30 to 60 days (see Fig. 5). These data suggest the possible hypothesis that nursing facilitated the contact of infant and mother during the early developmental periods.

The interpretation of all fear testing is complicated by the fact that all or most "fear" stimuli evoke many positive exploratory responses early in life and do not consistently evoke flight responses until the monkey is 40 to 50 days of age. Similar delayed maturation of visually induced fear responses has been reported for birds (*3*), chimpanzees (*20*), and human infants (*21*).

Because of apparent interactions between fearful and affectional developmental variables, a test was designed to trace the development of approach and avoidance responses in these infants. This test, described as the straight-alley test, was conducted in a wooden alley 8 feet long and 2 feet wide. One end of the alley contained a movable tray upon which appropriate stimuli were placed. The other end of the alley contained a box for hiding. Each test began with the monkey in a start box 1 foot in front of the hiding box; thus, the animal could maintain his original position, approach the stimulus tray as it moved toward him, or flee into the hiding box. The infants were presented with five stimuli in the course of five successive days. The stimuli included a standard cloth mother, a standard wire mother, a yellow cloth mother with the head removed, a blank tray, and a large black fear stimulus, shown in Fig. 9. The infants were tested at 5, 10, and 20 days of age, respectively, and then at 20-day intervals up to 160 days. Figure 10 shows the mean number of 15-second time



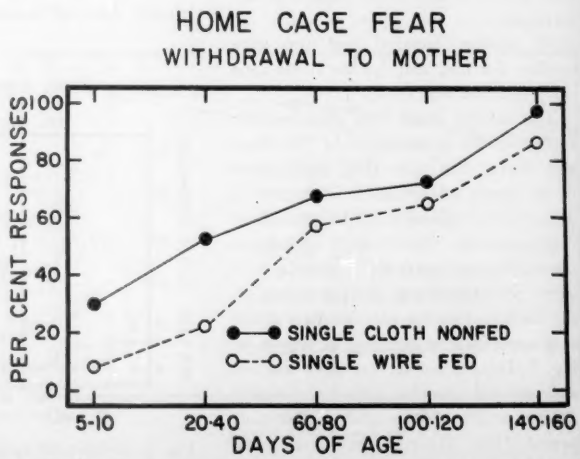


Fig. 6 (left). Time spent on single mother surrogates. Fig. 7 (right). Responsiveness to single surrogate mothers in fear tests.

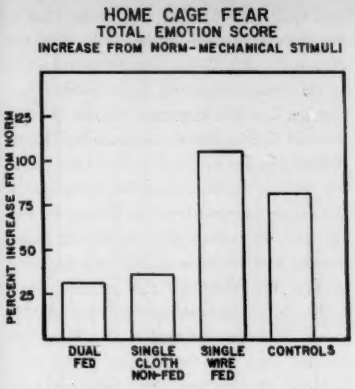


Fig. 8. Change in emotionality index in fear tests.

periods spent in contact with the appropriate mother during the 90-second tests for the two single-mother groups, and the responses to the cloth mother by four infants from the dual-mother group.

During the first 80 days of testing, all the groups showed an increase in response to the respective mother surrogates. The infants fed on the single wire mother, however, reached peak responsiveness at this age and then showed a consistent decline, followed by an actual avoidance of the wire mother. During test sessions 140 to 160, only one contact was made with the wire mother, and three of the four infants ran into the hiding box almost immediately and remained there for the entire test session. On the other hand, all of the infants raised with a cloth mother, whether or not they were nursed by her, showed a progressive increase in time spent in contact with their cloth mothers until approaches and contacts during the test sessions approached maximum scores.

The development of the response of flight from the wire mother by the group fed on the single wire mother is, of course, completely contrary to a derived-drive theory of affectional development. A comparison of this group with the group raised with a cloth mother gives some support to the hypothesis that feeding or nursing facilitates the early development of responses to the mother but that without the factor of contact comfort, these positive responses are not maintained.

The differential responsiveness to the cloth mother of infants raised with both mothers, the reduced emotionality of both the groups raised with cloth mothers in the home-cage fear tests, and the development of approach responses in the straight-alley test indicate that the cloth mother provides a haven of safety and security for the frightened infant. The affectional response patterns found in the infant monkey are unlike tropistic or even complex reflex responses; they resemble instead the diverse and pervasive patterns of response to his mother exhibited by the human child in the complexity of situations involving child-mother relationships.

The role of the mother as a source of safety and security has been demonstrated experimentally for human infants by Arsenian (*22*). She placed children 11 to 30 months of age in a strange room containing toys and other play objects. Half of the children were accompanied into the room by a mother or a substitute mother (a familiar nursery attendant), while the other half entered the situation alone. The children in the first group (mother present) were much less emotional and participated much more fully in the play activity than those in the second group (mother absent). With repeated testing, the security score, a composite score of emotionality and play behavior, improved for the children who entered alone, but it still fell far below that for the children who were accompanied by their mothers. In subsequent tests, the children from the mother-present group were placed in the test room alone, and there was a drastic drop in the security scores. Contrariwise, the introduction of the mother raised the security scores of children in the other group.

We have performed a similar series of open-field experiments, comparing monkeys raised on mother surrogates with control monkeys raised in a wire cage containing a cheesecloth blanket from days 1 to 14 and no cloth blanket subsequently. The infants were introduced into the strange environment of the open field, which was a room measuring 6 by 6 by 6 feet, containing multiple stimuli known to elicit curiosity-manipulatory responses in baby monkeys. The infants raised with single mother surrogates were placed in this situation twice a week for 8 weeks, no mother surrogate being present during one of the weekly sessions and the appropriate mother surrogate (the kind which the experimental infant had always known) being present during the other sessions. Four infants raised with dual mother surrogates and four control infants were subjected to similar experimental sequences, the cloth mother being present on half of the occasions. The remaining four "dual-mother" infants were given repetitive tests to obtain information on the development of responsiveness to each of the dual mothers in this situation. A cloth blanket was always available as one of the stimuli throughout the sessions. It should be emphasized that the blanket could readily compete with the cloth mother as a contact stimulus, for it was standard laboratory procedure to wrap the infants in soft cloth whenever they were removed from their cages for testing, weighing, and other required laboratory activities.

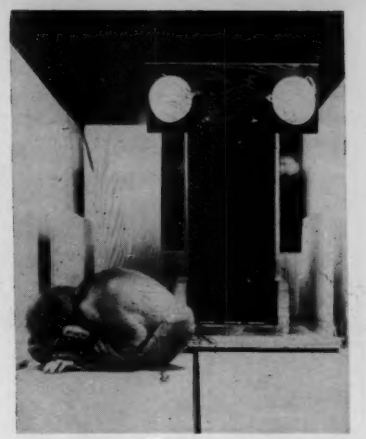


Fig. 9. Response to the fear stimulus in the straight-alley test.

As soon as they were placed in the test room, the infants raised with cloth mothers rushed to their mother surrogate when she was present and clutched her tenaciously, a response so strong that it can only be adequately depicted by motion pictures. Then, as had been observed in the fear tests in the home cage, they rapidly relaxed, showed no sign of apprehension, and began to demonstrate unequivocal positive responses of manipulating and climbing on the mother. After several sessions, the infants began to use the mother surrogate as a base of

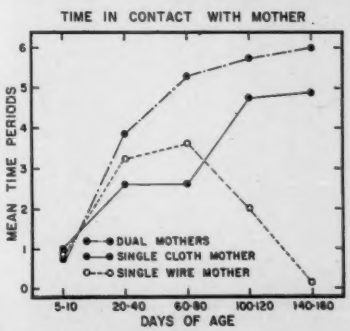


Fig. 10. Responsiveness to mother surrogates in the straight-alley tests.

Fig. 11. Subsequent response to cloth mother and stimulus in the open-field test.

operations, leaving her to explore and handle a stimulus and then returning to her before going to a new plaything. Some of the infants even brought the stimuli to the mother, as shown in Fig. 11. The behavior of these infants changed radically in the absence of the mother. Emotional indices such as vocalization, crouching, rocking, and sucking increased sharply. Typical response patterns were either freezing in a crouched position, as illustrated in Fig. 12, or running around the room on the hind feet, clutching themselves with their arms. Though no quantitative evidence is available, contact and manipulation of objects was frantic and of short duration, as opposed to the playful type of manipulation observed when the mother was present.

In the presence of the mother, the behavior of the infants raised with single wire mothers was both quantitatively and qualitatively different from that of the infants raised with cloth mothers. Not only did these infants spend little or no time contacting their mother surrogates but the presence of the mother did not reduce their emotionality. These differences are evident in the mean number of time periods spent in contact with the respective mothers, as shown in Fig. 13, and the composite emotional index for the two stimulus conditions depicted in Fig. 14. Although the infants raised with dual mothers spent considerably more time in contact with the cloth mother than did the infants raised with single cloth mothers, their emotional reactions to the presence and absence of the mother were highly similar, the composite emotional index being reduced by almost half when the mother was in the test situation. The infants raised with wire mothers were highly emotional under both conditions and actually showed a slight, though nonsignificant, increase in emotionality when the mother was present. Although some of the infants reared by a wire mother did contact her, their behavior was similar to that observed in the home-cage fear tests. They did not clutch and cling to their mother as did the infants with cloth mothers; instead, they sat on her lap and clutched themselves, or held their heads and bodies in their arms and engaged in convulsive jerking and rocking movements similar to the autistic behavior of deprived and institutionalized human children. The lack of exploratory and manipulatory behavior on the part of the infants reared with wire mothers, both in the presence and absence of the wire mother, was similar to that observed in the mother-absent condition for the infants raised with the cloth mothers, and such contact with objects as was made was of short duration and of an erratic and frantic nature. None of the infants raised with single wire mothers displayed the persistent and aggressive play behavior that was typical of many of the infants that were raised with cloth mothers.

The four control infants, raised without a mother surrogate, had approximately the same emotionality scores when the mother was absent that the other infants had in the same condition, but the control subjects' emotionality scores were significantly higher in the presence of the mother surrogate than in her absence. This result is not surprising, since recent evidence indicates that the cloth mother with the highly ornamental face is an effective fear stimulus

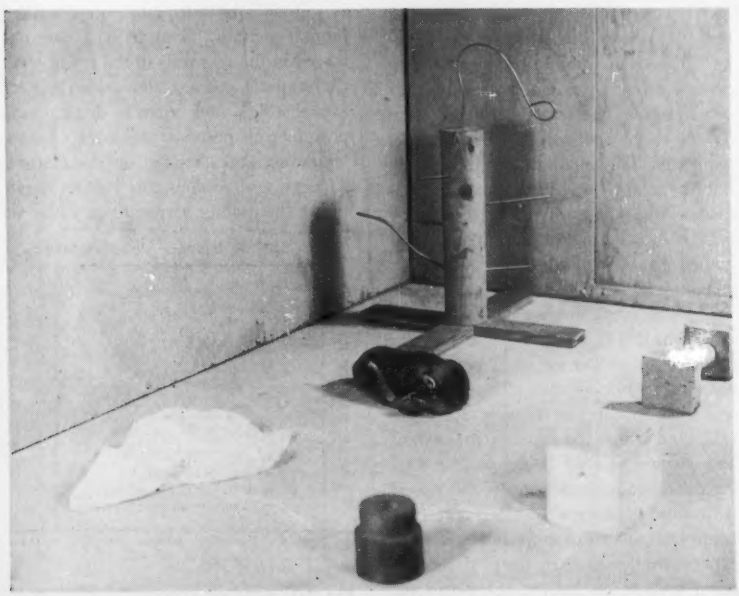
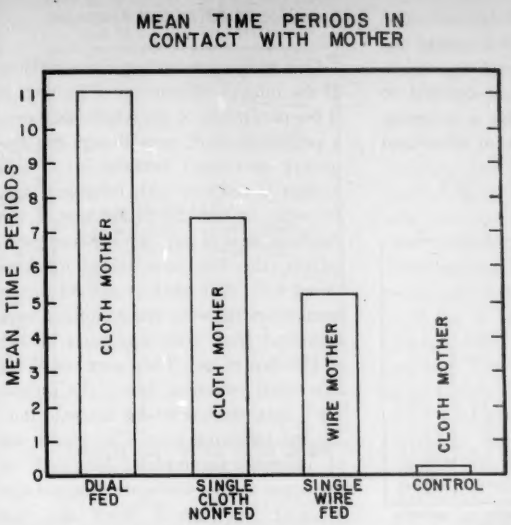


Fig. 12. Response in the open-field test in the absence of the mother surrogate.



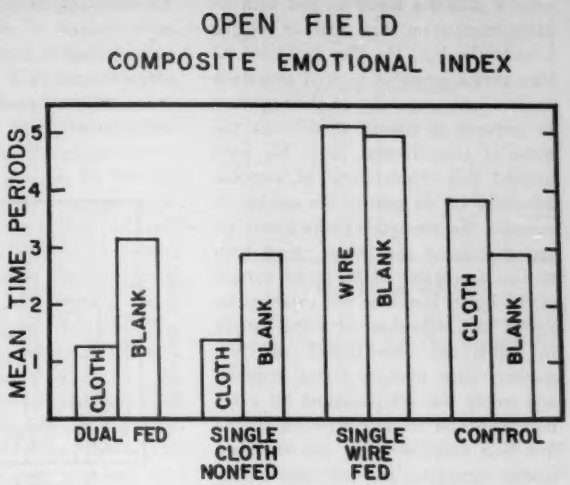
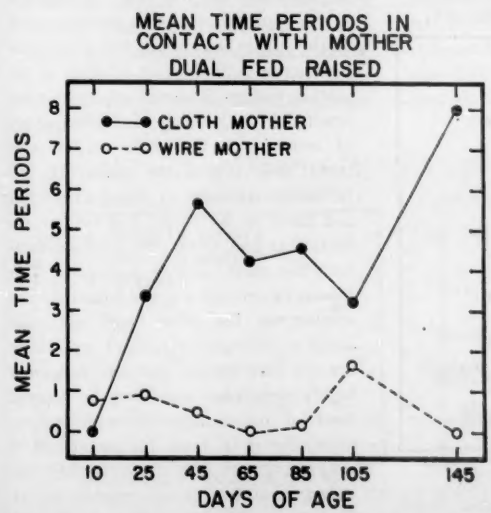


Fig. 13 (left). Responsiveness to mother surrogates in the open-field test. Fig. 14 (right). Emotionality index in testing with and without the mother surrogates.

for monkeys that have not been raised with her.

Further illustration of differential responsiveness to the two mother surrogates is found in the results of a series of developmental tests in the open-field situation, given to the remaining four "dual-mother" infants. These infants were placed in the test room with the cloth mother, the wire mother, and no mother present on successive occasions at various age levels. Figure 15 shows the mean number of time periods spent in contact with the respective mothers for two trials at each age level, and Fig. 16 reveals the composite emotion scores for the three stimulus conditions during these same tests. The differential responsiveness to the cloth and wire mothers, as measured by contact time, is evident by 20 days of age, and this systematic difference continues throughout 140 days of age. Only small differences in emotionality under the various conditions are evident during the first 85 days of age, although the presence of the cloth mother does result in slightly lower scores from the 45th day onward. However, at 105 and 145 days of age there is a considerable difference for the three conditions, the emotionality scores for the wire-mother and blank conditions showing a sharp increase. The heightened emotionality found under the wire-mother condition was mainly contributed by the two infants fed on the wire mother. The behavior of these two infants in the presence of the wire mother was similar to the behavior of the animals raised with a single wire mother. On the few occasions when contact with the wire mother was made, the infants did not attempt to cling to her; instead they would sit on her lap, clasp their heads and bodies, and rock back and forth.

In 1953 Butler (*23*) demonstrated that mature monkeys enclosed in a



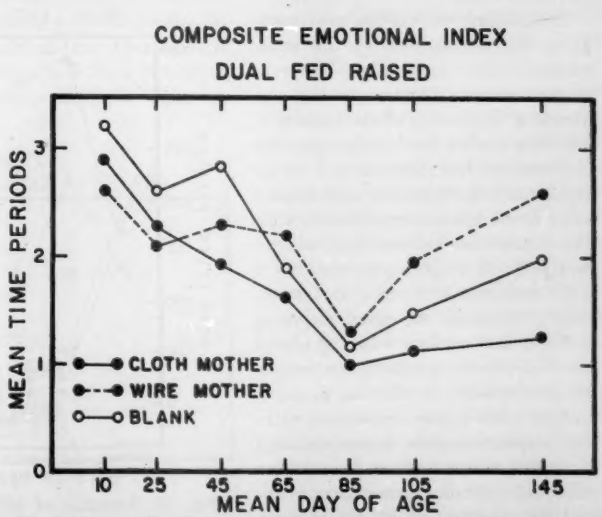


Fig. 15 (left). Differential responsiveness in the open-field test. Fig. 16 (right). Emotionality index under three conditions in the open-field test.

dimly lighted box would open and reopen a door for hours on end with no other motivation than that of looking outside the box. He also demonstrated that rhesus monkeys showed selectivity in rate and frequency of door-opening in response to stimuli of different degrees of attractiveness (*24*). We have utilized this characteristic of response selectivity on the part of the monkey to measure the strength of affectional responsiveness of the babies raised with mother surrogates in an infant version of the Butler box. The test sequence involves four repetitions of a test battery in which the four stimuli of cloth mother, wire mother, infant monkey, and empty box are presented for a 30-minute period on successive days. The first four subjects raised wth the dual mother surrogates and the eight infants raised with single mother surrogates were given a test sequence at 40 to 50 days of age, depending upon the availability of the apparatus. The data obtained from the three experimental groups and a comparable control group are presented in Fig. 17. Both groups of infants raised with cloth mothers showed approximately equal responsiveness to the cloth mother and to another infant monkey, and no greater responsiveness to the wire mother than to an empty box. Again, the results are independent of the kind of mother that lactated, cloth or wire. The infants raised with only a wire mother and those in the control group were more highly responsive to the monkey than to either of the mother surrogates. Furthermore, the former group showed a higher frequency of response to the empty box than to the wire mother.

In summary, the experimental analysis of the development of the infant monkey's attachment to an inanimate mother surrogate demonstrates the overwhelming importance of the variable of soft body contact that characterized the cloth mother, and this held true for the appearance, development, and maintenance of the infant-surrogate-mother tie. The results also indicate that, without the factor of contact comfort, only a weak attachment, if any, is formed. Finally, probably the most surprising finding is that nursing or feeding played either no role or a subordinate role in the development of affection as measured by contact time, responsiveness to fear, responsiveness to strangeness, and motivation to seek and see. No evidence was found indicating that nursing mediated the development of any of these responses, although there is evidence indicating that feeding probably facilitated the early appearance and increased the early strength of affectional responsiveness. Certainly feeding, in contrast to contact comfort, is neither a necessary nor a sufficient condition for affectional development.

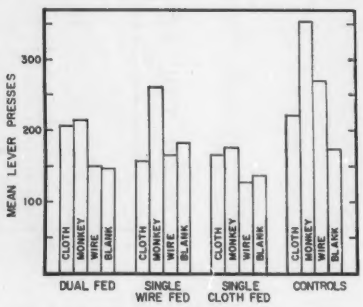


Fig. 17. Differential responses to visual exploration.

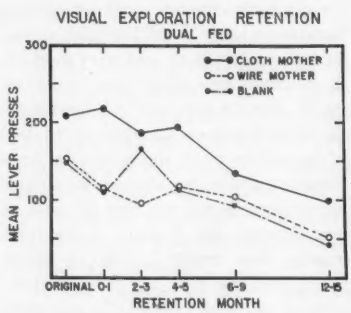


Fig. 18. Retention of differential visual-exploration responses.

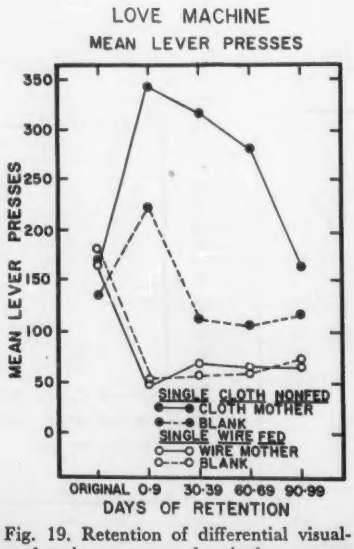


Fig. 19. Retention of differential visual-exploration responses by single-surrogate infants.

Retention of Affectional Responses

One of the outstanding characteristics of the infant's attachment to its mother is the persistence of the relationship over a period of years, even though the frequency of contact between infant and mother is reduced with increasing age. In order to test the persistence of the responsiveness of our "mother-surrogate" infants, the first four infant monkeys raised with dual mothers and all of the monkeys raised with single mothers were separated from their surrogates at 165 to 170 days of age. They were tested for affectional retention during the following 9 days, then at 30-day intervals during the following year. The results are of necessity incomplete, inasmuch as the entire mother-surrogate program was initiated less than 2 years ago, but enough evidence is available to indicate that the attachment formed to the cloth mother during the first 6 months of life is enduring and not easily forgotten.

Affectional retention as measured by the modified Butler box for the first 15 months of testing for four of the infants raised with two mothers is given in Fig. 18. Although there is considerable variability in the total response frequency from session to session, there is a consistent difference in the number of responses to the cloth mother as contrasted with responses to either the wire mother or the empty box, and there is no consistent difference between responses to the wire mother and to the empty box. The effects of contact comfort versus feeding are dramatically demonstrated in this test by the monkeys raised with either single cloth or wire mothers. Figure 19 shows the frequency of response to the appropriate mother surrogate and to the blank box during the preseparation period and the first 90 days of retention testing. Removal of the mother resulted in a doubling of the frequency of response to the cloth mother and more than tripled the difference between the responses to the cloth mother and those to the empty box for the infants that had lived with a single nonlactating cloth mother surrogate. The infants raised with a single lactating wire mother, on the other hand, not only failed to show any consistent preference for the wire mother but also showed a highly significant reduction in general level of responding. Although incomplete, the data from further retention testing indicate that the difference between these two groups persists for at least 5 months.

Affectional retention was also tested

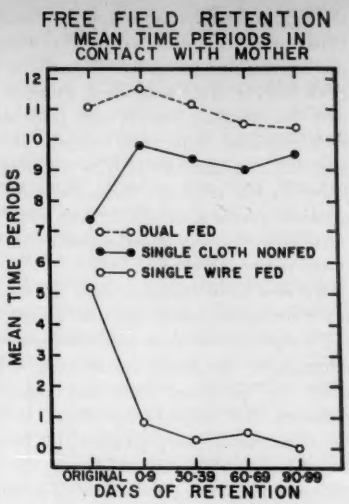


Fig. 20. Retention of responsiveness to mother surrogates in the open-field tests.

in the open field during the first 9 days after separation and then at 30-day intervals. Each test condition was run twice in each retention period. In the initial retention tests the behavior of the infants that had lived with cloth mothers differed slightly from that observed during the period preceding separation. These infants tended to spend more time in contact with the mother and less time exploring and manipulating the objects in the room. The behavior of the infants raised with single wire mothers, on the other hand, changed radically during the first retention sessions, and responses to the mother surrogate dropped almost to zero. Objective evidence for these differences are given in Fig. 20, which reveals the mean number of time periods spent in contact with the respective mothers. During the first retention test session, the infants raised with a single wire mother showed almost no responses to the mother surrogate they had always known. Since the infants raised with both mothers were already approaching the maximum score in this measure, there was little room for improvement. The infants raised with a single nonlactating cloth mother, however, showed a consistent and significant increase in this measure during the first 90 days of retention. Evidence for the persistence of this responsiveness is given by the fact that after 15 months' separation from their mothers, the infants that had lived with cloth mothers spent an average of 8.75 out of 12 possible time periods in contact with the cloth mother during the test. The incomplete data for retention testing of the infants raised with only a lactating wire mother or a nonlactating cloth mother indicates that there is little or no change in the initial differences found between these two groups in this test over a period of 5 months. In the absence of the mother, the behavior of the infants raised with cloth mothers was similar in the initial retention tests to that during the preseparation tests, but with repeated testing they tended to show gradual adaptation to the open-field situation and, consequently, a reduction in their emotionality scores. Even with this over-all reduction in emotionality, these infants had consistently lower emotionality scores when the mother was present.

At the time of initiating the retention tests, an additional condition was introduced into the open-field test: the surrogate mother was placed in the center of the room and covered with a clear Plexiglas box. The animals raised with cloth mothers were initially disturbed and frustrated when their efforts to secure and contact the mother were blocked by the box. However, after several violent crashes into the plastic, the animals adapted to the situation and soon used the box as a place of orientation for exploratory and play behavior.

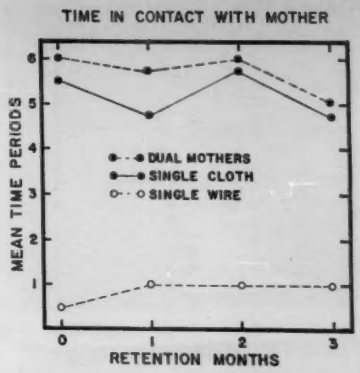


Fig. 22. Retention of responsiveness to mother surrogates in the straight-alley test.

In fact, several infants were much more active under these conditions than they were when the mother was available for direct contact. A comparison of the composite emotionality index of the babies raised with a single cloth or wire mother under the three conditions of no mother, surrogate mother, and surrogate-mother-box is presented in Fig. 21. The infants raised with a single cloth mother were consistently less emotional when they could contact the mother but also showed the effects of her visual presence, as their emotionality scores in the plastic box condition were definitely lower than their scores when the mother was absent. It appears that the infants gained considerable emotional security from the presence of the mother even though contact was denied.

In contrast, the animals raised with only lactating wire mothers did not show any significant or consistent trends during these retention sessions other than a general over-all reduction of emotionality, which may be attributed to a general adaptation, the result of repeated testing.

Affectional retention has also been measured in the straight-alley test mentioned earlier. During the preseparation tests it was found that the infants that had only wire mothers developed a general avoidance response to all of the stimuli in this test when they were about 100 days of age and made few, if any, responses to the wire mother during the final test sessions. In contrast, all the infants raised with a cloth mother responded positively to her. Maternal separation did not significantly change the behavior of any of the groups. The babies raised with just wire mothers continued to flee into the hiding booth in the presence of the wire mother, while all of the infants raised with

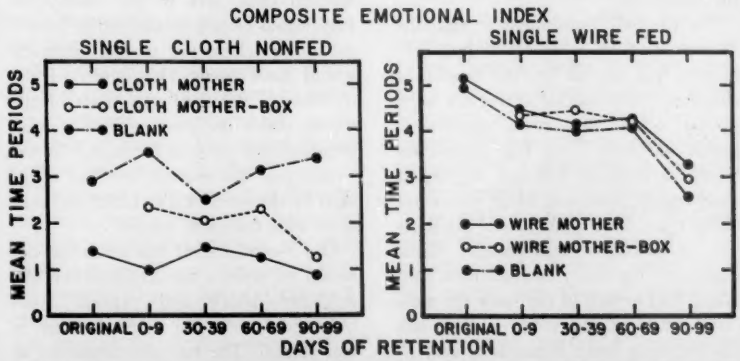


Fig. 21. Emotionality index under three conditions in the open-field retention tests.

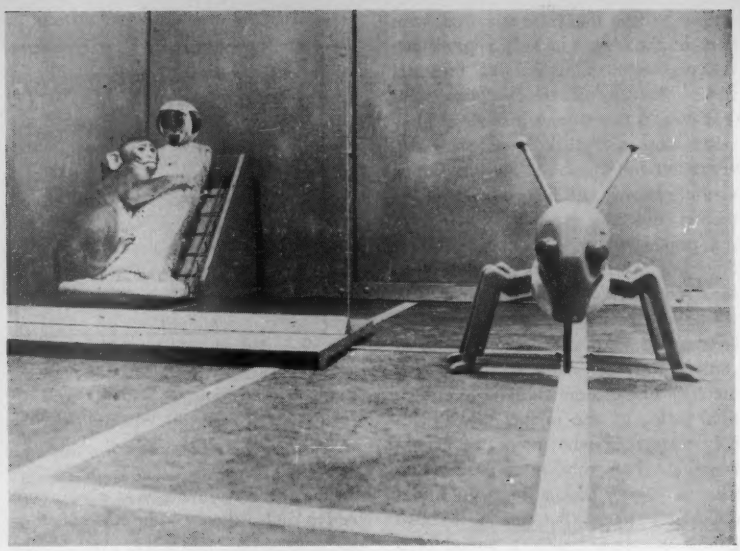


Fig. 23. Typical response to cloth mother in the modified open-field test.

cloth mothers continued to respond positively to the cloth mother at approximately the same level as in the preseparation tests. The mean number of time periods spent in contact with the appropriate mother surrogates for the first 3 months of retention testing are given in Fig. 22. There is little, if any, waning of responsiveness to the cloth mother during these 3 months. There appeared to be some loss of responsiveness to the mother in this situation after 5 to 6 months of separation, but the test was discontinued at that time as the infants had outgrown the apparatus.

The retention data from these multiple tests demonstrate clearly the importance of body contact for the future maintenance of affectional responses. Whereas several of the measures in the preseparation period suggested that the infants raised with only a wire mother might have developed a weak attachment to her, all responsiveness disappeared in the first few days after the mother was withdrawn from the living-cage. Infants that had had the opportunity of living with a cloth mother showed the opposite effect and either became more responsive to the cloth mother or continued to respond to her at the same level.

These data indicate that once an affectional bond is formed it is maintained for a very considerable length of time with little reinforcement of the contact-comfort variable. The limited data available for infants that have been separated from their mother surrogates for a year suggest that these affectional responses show resistance to extinction similar to the resistance previously demonstrated for learned fears and learned pain. Such data are in keeping with common observation of human behavior.

It is true, however, that the infants raised with cloth mothers exhibit some absolute decrease in responsiveness with time in all of our major test situations. Such results would be obtained even if there were no true decrease in the strength of the affectional bond, because of familiarization and adaptation resulting from repeated testing. Therefore, at the end of 1 year of retention testing, new tests were introduced into the experimental program.

Our first new test was a modification of the open-field situation, in which basic principles of the home-cage fear test were incorporated. This particular choice was made partly because the latter test had to be discontinued when the mother surrogates were removed from the home cages.

For the new experiment a Masonite floor marked off in 6- by 12-inch rectangles was placed in the open-field chamber. Both mother surrogates were placed in the test room opposite a plastic start-box. Three fear stimuli, selected to produce differing degrees of emotionality, were placed in the center of the room directly in front of the start-box in successive test sessions. Eight trials were run under each stimulus condition, and in half of the trials the most direct path to the cloth mother was blocked by a large Plexiglas screen, illustrated in Fig. 23. Thus, in these trials the infants were forced to approach and bypass the fear stimulus or the wire mother, or both, in order to reach the cloth mother. Following these 24 trials with the mothers present, one trial of each condition with both mothers absent was run, and this in turn was followed by two trials run under the most emotion-provoking condition: with a mechanical toy present and the direct path to the mother blocked.

We now have complete data for the first four infants raised with both a cloth and a wire mother. Even with this scanty information, the results are obvious. As would be predicted from our other measures, the emotionality scores for the three stimuli were significantly different and these same scores were increased greatly when the direct path to the mother was blocked. A highly significant preference was shown for the cloth mother under both conditions (direct and blocked path), although the presence of the block did increase the number of first responses to the wire mother from 3 to 10 percent. In all cases this was a transient response and the infants subsequently ran on to the cloth mother and clung tightly to her. Objective evidence for this overwhelming preference is indicated in Fig. 24, which shows the mean number of time periods spent in contact with the two mothers. After a number of trials, the infants would go first to the cloth mother and then, and only then, would go out to explore, manipulate, and even attack and destroy the fear stimuli. It was as if they believed that their mother would protect them, even at the cost of her life —little enough to ask in view of her condition.

The removal of the mother surrogates from the situation produced the predictable effect of doubling the emotionality index. In the absence of the mothers, the infants would often run to the Plexiglas partition which formerly had blocked their path to the mother, or they would crouch in the corner behind the block where the mother normally would have been. The return of the mothers in the final two trials of the test in which the most emotion-evoking situation was presented resulted in behavior near the normal level, as measured by the emotionality index and contacts with the cloth mother.

Our second test of this series was designed to replace the straight-alley test described above and provide more quantifiable data on responsiveness to fear stimuli. The test was conducted in an alley 8 feet long and 2 feet wide.

At one end of the alley and directly behind the monkeys' restraining chamber was a small stimulus chamber which contained a fear object. Each trial was initiated by raising an opaque sliding door which exposed the fear stimulus. Beginning at a point 18 inches from the restraining chamber, the alley was divided lengthwise by a partition; this provided the infant with the choice of entering one of two alleys.

The effects of all mother combinations were measured; these combinations included no mothers, two cloth mothers, two wire mothers, and a cloth and a wire mother. All mother conditions were counterbalanced by two distance conditions—distances of 24 and 78 inches, respectively, from the restraining chamber. This made it possible, for example, to provide the infant with the alternative of running to the cloth mother which was in close proximity to the fear stimulus or to the wire mother (or no mother) at a greater distance from the fear stimulus. Thus, it was possible to distinguish between running to the mother surrogate as an object of security, and generalized flight in response to a fear stimulus.

Again, the data available at this time are from the first four infants raised with cloth and wire mothers. Nevertheless, the evidence is quite conclusive. A highly significant preference is shown for the cloth mother as compared to the wire mother or to no mother, and this preference appears to be independent of the proximity of the mother to the fear stimulus. In the condition in which two cloth mothers are present, one 24 inches from the fear stimulus and the other 78 inches from it, there was a preference for the nearest mother, but the differences were not statistically significant. In two conditions in which no cloth mother was present and the infant had to choose between a wire mother and no mother, or between two empty chambers, the emotionality scores were almost twice those under the cloth-mother-present condition.

No differences were found in either of these tests that were related to previous conditions of feeding—that is, to whether the monkey had nursed on the cloth or on the wire mother.

The results of these two new tests, introduced after a full year's separation of mother surrogate and infant, are comparable to the results obtained during the preseparation period and the early retention testing. Preferential responses still favored the cloth as compared to the wire mother by as much as 85 to 90 percent, and the emotionality scores showed the typical 2:1 differential ratio with respect to mother-absent and mother-present conditions.

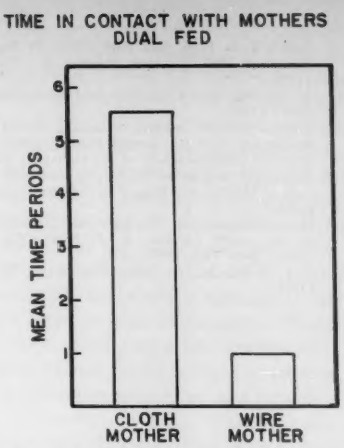


Fig. 24. Differential responsiveness in the modified open-field test.

The researches presented here on the analysis of two affectional variables through the use of objective and observational techniques suggest a broad new field for the study of emotional development of infant animals. The analogous situations and results found in observations and study of human infants and of subprimates demonstrate the apparent face validity of our tests. The reliability of our observational techniques is indicated, for example, by the correlation coefficients computed for the composite emotional index in the open-field test. Four product-moment correlation coefficients, computed from four samples of 100 observations by five different pairs of independent observers over a period of more than a year, ranged from .87 to .89.

Additional Variables

Although the overwhelming importance of the contact variable has been clearly demonstrated in these experiments, there is reason to believe that other factors may contribute to the development of the affectional response pattern. We are currently conducting a series of new experiments to test some of these postulated variables.

For example, Bowlby (*14*) has suggested that one of the basic affectional variables in the primate order is not just contact but *clinging* contact. To test this hypothesis, four infant monkeys are being raised with the standard cloth mother and a flat inclined plane, tightly covered with the same type of cloth. Thus, both objects contain the variable of contact with the soft cloth, but the shape of the mother tends to maximize the clinging variable, while the broad flat shape of the plane tends to minimize it. The preliminary results for differences in responsiveness to the cloth mother and responsiveness to the inclined plane under conditions that produce stress or fear or visual exploration suggest that clinging as well as contact is an affectional variable of considerable importance.

Experiments now in progress on the role of rocking motion in the development of attachment indicate that this may be a variable of measurable importance. One group of infants is being raised on rocking and stationary mothers and a second group, on rocking and stationary inclined planes. Both groups of infants show a small but consistent preference for the rocking object, as measured in average hours spent on the two objects.

Preliminary results for these three groups in the open-field test give additional evidence concerning the variable of clinging comfort. These data revealed that the infants raised with the standard cloth mother were more responsive to their mothers than the infants raised with inclined planes were to the planes.

The discovery of three variables of measurable importance to the formation and retention of affection is not surprising, and it is reasonable to assume that others will be demonstrated. The data so far obtained experimentally are in excellent concordance with the affectional variables named by Bowlby (*14*). We are now planning a series of studies to assess the effects of consistency and inconsistency with respect to the mother surrogates in relation to the clinical concept of rejection. The effects of early, intermediate, and late maternal deprivation and the generalization of the infant-surrogate attachment in social development are also being investigated. Indeed, the strength and stability of the monkeys' affectional responses to a mother surrogate are such that it should be practical to determine the neurological and biochemical variables that underlie love.

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Amino Acid Metabolism in Mammalian Cell Cultures

Harry Eagle

A number of cell lines derived from normal and malignant tissues have now been serially propagated in culture. These may be grown adherent to a glass surface and overlaid with a fluid medium, or they may be grown in suspension; but in either case the opportunity is presented for the study of metabolism at the cellular level in a system which operationally resembles bacterial cultures in most essential respects. The cells and the medium can be separately analyzed, balance experiments can be set up, metabolic processes can be examined qualitatively and quantitatively under controlled conditions, and the corresponding enzymatic activities can be explored in cell-free extracts.

A relatively limited number of metabolites have been shown to suffice for the apparently indefinite propagation of all the human cell lines so far studied. The minimal medium, in which every component is demonstrably essential, is listed in Table 1 and includes 29 components: 13 amino acids, 8 vitamins, 6 ionic species, glucose, and serum protein (*1, 2*). The role of the serum protein is not entirely clear. Although a few cell lines have been serially propagated in a protein-free medium (*3*), serum protein is required by most mammalian cell cultures. In monolayer cultures, the protein plays a role in the adhesion of the cells to glass (*4*). However, its essentiality in suspension cultures indicates that this is not its only function, and it seems reasonable to assume that it acts in part as a carrier of as yet unidentified growth factors which are bound to the protein, and which are slowly released into the medium.

The present article, dealing with the amino acid metabolism of these cultured cells, is a progress report rather than a review and in large part summarizes studies from a single laboratory. The enormous body of information available with respect to amino acid metabolism in bacterial cultures (*5, 6*) has served as a stimulus and prototype for the studies here reported. The relevant findings in bacterial systems have not been referred to in detail, only because that important exercise in comparative biochemistry is beyond the scope of the present report.

Nutritionally Essential Amino Acids

The classic experiments of Rose and his coworkers (*7*) have shown that eight amino acids (isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine) suffice for nitrogen balance in feeding experiments in man. In contrast, every cell culture so far examined, whether human or animal (*8*) in origin, and whether deriving from normal or malignant tissue (*9*), has required at least 13 amino acids for survival and growth. Over and above the eight amino acids required for nitrogen balance, these cell cultures require arginine, cyst(e)ine, glutamine, histidine, and tyrosine, and on the omission of any one of these, the cells degenerate and die. In their early stages these degenerative processes are reversible. This presents an opportunity to explore the intimate structural derangement caused by specific amino acid deficiences, and the reparative processes which occur on restoration of these amino acids to the medium.

None of the D-amino acids substitute for the L-isomer (*8*) except for D-cystine, and this apparently acts by mobilizing cyst(e)ine residues bound to the serum protein of the medium. (This is discussed below.) Dipeptides were found to be active, substituting for both component amino acids (*10*). Recent experiments indicate that, although dipeptides are hydrolyzed extracellularly by serum peptidases, and perhaps by cell-derived peptidases, some of the dipeptide is transported into the cell and there hydrolyzed.

A number of keto acids and other amino acid congeners have been tested with respect to their ability to substitute for the corresponding amino acid (*11*). The results with several human and animal cell lines are summarized in Table 2. The cells contain a wide variety of transaminases (*12*), and, as determined in feeding experiments in rats (*5*), most of these keto acids do in fact substitute for the corresponding amino acid.

Of particular interest is the fact that, with all the human cell lines studied, citrulline substituted for arginine, while ornithine was inactive [Table 2; see also (*13*)]. Attempts to encourage citrulline biosynthesis by progressive removal of

The author is chief of the laboratory of cell biology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Md.

citrulline from a medium containing ornithine have to date been unsuccessful.

A number of possibilities may be considered in explanation of the fact that at least five amino acids which are not required for nitrogen balance are nevertheless essential for the survival and growth of cells in culture.

1) *Loss of biosynthetic mechanisms during prolonged growth in vivo.* The enzymatic systems which, in vivo, permit the biosynthesis of arginine, cyst(e)ine, glutamine, histidine, and tyrosine may have been lost, in whole or in part, during the hundreds of generations of rapid growth in vitro. To assess this possibility, cells deriving from monkey kidney, monkey testis, and rabbit embryonic tissues were examined with respect to their amino acid requirements in first culture passage, within 24 to 48 hours after their isolation from the animal host and prior to extensive multiplication (*11, 14*). All 13 amino acids required by long-term cell cultures were necessary also for the survival and growth of these first-passage cells. The requirement for 13 amino acids rather than eight is therefore not due to loss of biosynthetic mechanisms in the course of prolonged growth in culture, but these experiments do not exclude the possibility that the necessary enzymes are lost from the cells within the first 48 hours after their removal from the animal.

2) *Lack of appropriate precursors or cofactors (the role of folinic acid in glycine synthesis).* A second possibility is that cultured cells retain the capacity to synthesize these five amino acids but that this is not evidenced in culture for lack of appropriate precursors or cofactors. This possibility is illustrated in the biosynthesis of glycine by monkey kidney cells in primary culture. For optimum growth, these cells require glycine (*14, 15*) because of a partial block in the conversion of serine to glycine (*16*), and that glycine requirement has been shown to be eliminated by the provision of folinic acid (*17*). The primary block in the biosynthesis of glycine by this cell culture is apparently in the reduction of folic acid to the metabolically active cofactor. However, no simple precursor has yet been found which can be used by cultured cells in lieu of preformed arginine, cyst(e)ine, glutamine, histidine, or tyrosine, and no cofactor has been recognized which, as in the case of folinic acid and glycine, will stimulate that biosynthesis by cultured cells.

3) *Limited biosynthetic capacity, sufficient for survival but not for growth.* As a third possible explanation for the essential nutritional role of arginine, cyst(e)ine, glutamine, histidine, and tyrosine in cell cultures, it is possible that all mammalian cells, both in vivo and in vitro, have a limited capacity for the biosynthesis of these amino acids which could suffice for maintenance and nitrogen balance in whole-animal feeding experiments but which is inadequate for the rapid growth characteristic of cell cultures. Such partial synthesis has been demonstrated under certain conditions for glutamine, cyst(e)ine and tyrosine.

Glutamine synthesis. Although glutamic acid at physiological levels usually does not substitute for glutamine in these cell cultures, experiments with C^{14}-labeled glutamic acid and N^{15}-ammonia have shown (*18*) that the cells do have a limited capacity to make glutamine from these precursors. Since glutamic acid, in turn, is formed to only a limited extent from glucose, glutamine is an essential amino acid for all of the serially propagated human cell cultures so far studied. However, monkey kidney cells in primary passage can use glutamic acid or glutamine interchangeably (*14*), and in these cultures the minor biosynthesis of glutamic acid from glucose permits prolonged survival, and occasionally limited growth, in a medium lacking both glutamine and glutamic acid. A similar limited biosynthesis by human cells could account for the fact that glutamine is not necessary for nitrogen balance in short-term feeding experiments in man.

Although it is not relevant to the main thread of this discussion, it is of interest to note that with every cell line so far examined, high levels of glutamic acid substitute for glutamine (*19*). DeMars has made the important observation that at these high concentrations the cells form greatly increased amounts of glutamine synthetase (*20, 21*). This increased enzyme formation was product-inhibited—that is, the formation of glutamine synthase was inhibited by the presence of glutamine. Having formed the enzyme, the cells can then grow at low levels of glutamic acid for long periods, and perhaps indefinitely (*21*). This may be the first case of enzyme induction in serially propagated mammalian cell cultures.

Monkey kidney cells in primary culture, which can utilize glutamic acid and glutamine interchangeably, were found to have a glutamine synthetase activity

Table 1. Minimum essential medium* for cultivation of mammalian cells in either monolayer or suspension. The concentrations of most of the amino acids are greater than those originally recommended (*1*) and the relative amounts conform more closely to the protein composition of cultured human cells (*23*). This permits the cultures to be kept for somewhat longer periods without refeeding. The concentration of some of the salts has been rounded off. In using this medium for the growth of cells in suspension, Ca^{++} should be omitted or greatly reduced in order to minimize clumping (see *43*), and the concentration of NaH_2PO_4 may be increased tenfold for more effective buffering (*43*).

Compound	Concentration (m*M*)	Concentration (mg/lit.*)	Compound	Concentration (m*M*)	Concentration (mg/lit.*)
L-*Amino Acids*			*Salts*		
Arginine	0.6	105	NaCl	116	6800
Cystine	0.1	24	KCl	5.4	400
Glutamine*	2.0	292	$CaCl_2$	1.8 (0)†	200 (0)†
Histidine	0.2	31	$MgCl_2 \cdot 6H_2O$	1.0	200
Isoleucine	0.4	52	$NaH_2PO_4 \cdot 2H_2O$	1.1 (11)†	150 (1500)†
Leucine	0.4	52	$NaHCO_3$†‡	23.8	2000†
Lysine	0.4	58	*Vitamins**		
Methionine	0.1	15	Choline		1
Phenylalanine	0.2	32	Folic acid		1
Threonine	0.4	48	Inositol		2
Tryptophan	0.05	10	Nicotinamide		1
Tyrosine	0.2	36	Pantothenate		1
Valine	0.4	46	Pyridoxal		1
*Carbohydrate**			Riboflavin		0.1
Glucose	5.5	1000	Thiamine		1
			Serum Protein§		
			Whole or dialyzed serum, 5 to 10%		

* The fact that some of the amino acids can be replaced by such immediate precursors as the corresponding keto acids (*11*), that the vitamins can be replaced by the corresponding cofactors (*44*), or that a number of carbohydrates will substitute for glucose (*45*) does not change the minimum number of essential growth factors but relates only to the form in which they may be supplied. Conversely, the fact that bicarbonate, for example, is not an essential nutrilite for any of the serially propagated lines so far examined has no bearing on its essential metabolic role and means only that CO_2 is formed in adequate amounts from other components of the minimal medium—for example, glucose.

† In suspension cultures (see *43*).

‡ With small cell populations, the concentration of $NaHCO_3$ may be reduced from 0.20 to, for example, 0.04 percent in order to minimize the alkalinization of the medium in the early stages of growth.

§ Optional supplementation is as follows: (i) "nonessential" amino acids (alanine, asparagine, aspartic acid, glycine, glutamic acid, proline, serine), each at 0.1 m*M*; (ii) sodium pyruvate (1 m*M*). Of these, asparagine, serine, glycine, and pyruvate have proved necessary for the growth of certain cell lines, in a dialyzed serum medium, and serine is similarly required for the growth of single cells.

Table 2. Growth response of cultured cells to keto acid analogs of essential amino acids and related compounds (*11*).

Amino acid	Keto acid analog*	Growth response† of		
		Human cell lines‡	Mouse cell lines§	Rats (*5*)
L-Histidine	β-Imidazolyl-pyruvic	++	++	+
L-Isoleucine	α-Keto-β-methylvaleric	++	++	+
L-Leucine	α-Ketoisocaproic	++	++	+
L-Methionine	α-Keto-γ-methiolbutyric	++	++	+
L-Phenylalanine	Phenylpyruvic	++	++	+
L-Tyrosine	*p*-Hydroxyphenylpyruvic	±		+
L-Valine	α-Ketoisovaleric	++	++	+
L-Arginine	α-Keto-δ-guanidinovaleric	0	0	0
L-Threonine	α-Keto-β-hydroxybutyric	0		
L-Tryptophan	β-Indolylpyruvic	0		+
Other analogs substituting for amino acid in growth of human cell lines				
Arginine	Citrulline	+ to ++		
Histidine	Imidazole lactic acid	±		

* Other inactive analogs are as follows. Arginine: α-ketocarbamidovaleric acid, L-ornithine, guanidine, guanidoacetic acid. Histidine: L-histidinol, L-histidinol phosphate, imidazole glycerol, imidazole glycerol phosphate, imidazole acetol phosphate. Leucine: leucic acid. Lysine: DL-pipecolic acid. Methionine: DL-homocystine (+ serine), DL-homoserine (+ cystine or inorganic sulfur). Valine: α-hydroxyisovaleric acid.
† (++) Growth rate of cultures equal to that obtained with amino acid: (+) growth rate approximately half that observed with amino acid; (±) definite but slight growth; (0) no significant growth response.
‡ HeLa, KB, conjunctiva, liver, Detroit 116P.
§ Mouse fibroblast (strain L-929) and sarcoma 180.

of the same order of magnitude as that of glutamic-acid–adapted HeLa cells (*22*).

Provision of cyst(e)ine in a "cystine-free" medium. Four general pathways for the provision of cyst(e)ine have proved to be used by cultured human cells (*2*), including *de novo* biosynthesis. That biosynthesis alone does not, however, suffice for growth.

One pathway involves the release of preformed cysteine from cystathionine. L-Homocystine is also active, but only in part by virtue of the condensation of homocysteine with L-serine to give L-cystathionine. In addition, as is discussed in a following paragraph, it serves to dissociate cysteine residues bound to the serum protein of the medium. The degree to which methionine can be used to synthesize cysteine by way of homocysteine is under present study.

Cultured human cells contain a large pool of taurine and glutathione (*23*). When they are grown in a cyst(e)ine-free medium, that glutathione, unlike the taurine, largely disappears (*11*). Its quantitative utilization for the provision of cystine would permit a 50- to 75-percent increase in cell protein. It remains to be seen whether, as in *Escherichia coli* (*24*), there is a similar cannibalization of dispensable cell proteins.

Table 3. The biosynthesis of the "nonessential" amino acids. The numbers in the body of the table represent (i) specific activity per C atom, or (ii) atoms percent excess, in each case referred to that of the precursor as 100, it being assumed that all incorporation is into newly synthesized protein. (After *17, 18*).

Amino acid synthesized by cell	Labeled precursors in medium						
	Glucose-U-C^{14}	Serine-U-C^{14}	Glutamine-U-C^{14}	Glutamic-U-C^{14}	Glutamine-amide N^{15}	Glutamic-N^{15}	$N^{15}H_3$
	Carbon skeleton				Amide N	α-NH_2	
Alanine	76	.65	7	7		80	4
Glycine	77	66		7		75	5
Serine	78	65	2	10		76	4
Asparagine					84		
Aspartic	11	.66	68	58		78	6
Glutamine					100		
Glutamic	6	.08	62	84		83	4
Proline	7	.26	39	27		58	
Cyst(e)ine	22–47	22–32		2			

The serum protein which must be added to the medium for the sustained growth of almost all mammalian cell lines (*1*) binds significant amounts of amino acids, which are released on boiling or on treatment with trichloroacetic acid (*11*). Bound cyst(e)ine is present in dialyzed human and horse serum at a concentration of at least 0.03m*M*, and the slow but continuing growth which may be observed in a cyst(e)ine-free medium (the rate increasing with the concentration of serum) is due in part to the mobilization of this bound cyst(e)ine. The marked stimulatory effect of reduced inorganic sulfur compounds (S^{--}, $S_2O_3^{--}$, $S_2O_4^{--}$, SO_3^{--}) on cell growth in a cyst(e)ine-free medium is similarly due to the fact that they promote the release of the bound cystine residues from the serum protein (*11*). As shown by experiments with $Na_2S^{35}O_3$, the inorganic S is not itself used in cyst(e)ine biosynthesis (*11*), unlike the case of *E. coli* (*24*). D-Cystine and D-homocystine also promote growth in a cystine-free medium, as will glutathione, thioglycollate, cysteamine, and cystamine (*11*). These compounds mobilize bound cyst(e)ine from serum protein; in addition, some may yield NaSH by the action of a cellular desulfhydrase.

Over and above the utilization of preformed cystine, or of closely related compounds such as glutathione and cystathionine, the cell can synthesize limited amounts of cyst(e)ine from glucose (*11*) (see Table 3). The source of the sulfur in this limited biosynthesis, which of itself does not suffice for survival and growth, is probably methionine, by way of homocystine.

Biosynthesis of tyrosine from phenylalanine. There is another example of a limited amino acid biosynthesis which might suffice for nitrogen balance and maintenance but which does not suffice for the sustained growth of cell cultures. A HeLa cell variant appeared spontaneously, characterized by a fibroblast-like appearance, which overgrew the parent strain. This variant culture, unlike any other cell line so far examined, was able to effect the hydroxylation of phenylalanine to tyrosine to a minor but significant degree (*25*). The reaction was completely inhibited in the presence of tyrosine—another example of a product-inhibited amino acid biosynthesis. Despite their ability to make significant amounts of tyrosine, these altered cells could not survive in a tyrosine-free medium, and added tyrosine was necessary for survival and growth. None of the other cell lines so far ex-

amined have been able to effect this hydroxylation, even in trace amounts, at least under the conditions of these experiments and in the medium of Table 1.

4) *The possible physiologic significance of the requirement of 13 amino acids.* In explaining the fact that cultured cells require arginine, cyst(e)ine, glutamine (or a precursor amino acid), histidine, and tyrosine, a final possibility may be considered: that most body cells do in fact require all five of these amino acids. It could be that they are unnecessary for nitrogen balance in feeding experiments in man only because they are supplied either by the action of the intestinal flora on the other amino acids or by the metabolic action of, for example, the liver.

Biosynthesis of the "Nonessential" Amino Acids

Of the amino acids which are nutritionally nonessential, the carbon skeletons of three (alanine, serine, and glycine) derive primarily from glocose, while four (asparagine, aspartic acid, glutamic acid, and proline) derive their carbon primarily from glutamine (*17, 18*). This dissociation is, however, not complete (see Table 3). In a medium containing both glucose and glutamine, 2 to 7 percent of the alanine and serine carbons derive from glutamine, and, conversely, amino acids of the glutamine family derive 5 to 11 percent of their carbon from products of glucose metabolism. The biosynthesis of cyst(e)ine is discussed above.

The specific source of the α-amino nitrogen of the eight nutritionally nonessential amino acids is now under study. Glutamic acid, either directly or by way of aspartic acid, is apparently the primary source of the α-NH_2 group of alanine, serine, glycine, asparagine, and proline. Free ammonia, which derives almost entirely from the amide group of glutamine, when cells are grown in the minimal medium of Table 1, is used by the cells to only an insignificant degree for the biosynthesis of either amino acids, purines, or pyrimidines (*18, 26–28*). (The only exception is the biosynthesis of glutamine from glutamic acid.)

Particular interest attaches to the biosynthesis of asparagine. In a minimal medium its carbon skeleton has been found to derive from glutamine, presumably by way of aspartic acid, while its amide nitrogen derives primarily from the amide nitrogen of glutamine (*27*). There is no present information as to the exact metabolic steps involved.

Vitamin B_6 has been found to play an essential role in the synthesis of alanine, serine, glycine, and proline (*29*). In cells depleted of pyridoxal, the concentration of these amino acids in the cell pool was markedly reduced (*30*), and growth, which ceases in the vitamin-deficient cell, could be restored by the addition to the medium of these nonessential amino acids (*29, 30*).

The designation of eight amino acids as nutritionally nonessential requires qualification on several scores. As indicated in Table 4, at least one cell line has shown a requirement for asparagine (*31*) over and above the requirement for glutamine. A rabbit fibroblast has been found to require serine (*32*), as did cells from the limb-buds of 22-day-old rabbit embryos (*11*), and monkey kidney cells in primary culture require glycine for optimal growth (*14, 15*).

There is another situation in which normally nonessential amino acids regularly become essential for the optimum growth and even for the survival of serially propagated cells. The minimal medium of Table 1, supplemented with 3- to 5-percent dialyzed serum, suffices for the indefinite growth of all the serially propagated human cell cultures so far examined, provided that a sufficiently large inoculum is used. However, when a minute cell population is placed in a relatively large volume of fluid, as in cloning experiments (*33*), that basal medium is usually no longer effective. The rate of growth of the clones is markedly reduced, and the cloning efficiency—that is, the proportion of cells which grew out to form visible colonies—is sometimes also greatly reduced (*34*). The growth of these small cell populations has been shown to be restored to normal levels by the addition either of whole serum, of higher concentrations of dialyzed serum, or of the nonessential amino acids (*34*). In most of the experiments the complete mixture of the nutritionally nonessential amino acids could be replaced by a single amino acid, serine. Glycine was usually only partially effective, and this probably reflects the limited degree to which glycine can be used by these cells for the biosynthesis of serine (*16*).

Preliminary results indicate that the major factor involved in this anomalous requirement for a "nonessential" amino acid, serine, by small cell populations is the loss of serine from the cell pool into the medium at a rate which exceeds the biosynthetic capacity of the cell (*26*).

Amino Acid Pool

All the cultured human cells examined to date have been found to contain a significant amino acid pool (*23*), the composition of which is essentially similar to that in animal tissues. Glutathione, taurine, glutamine, ammonia, and glutamic acid are present in largest amounts and together constitute approximately 60 percent of the total pool amino acids.

At concentrations in the medium comparable to those in the body fluids,

Table 4. Nutritional and metabolic differences in cell cultures.

Cell strain	Unusual nutritional requirement	Unusual metabolic activity	Reference
Walker carcinosarcoma (256)	Asparagine		(*31*)
Rabbit fibroblast (RM3) and embryonic limb-bud cells	Serine		(*17, 32*)
Monkey kidney cells in primary culture	Glycine	Aspartic } → glutamine Glutamic }	(*14, 15*) (*14*)
Mouse fibroblast (strain "L")		Biosynthesis of inositol in amounts sufficient for growth	(*46*)
Mouse leukemia (strain 388)	Pyruvate		(*47*)
Mouse embryonic cells	Pyruvate		(*11*)
HeLa "variant"		Phenylalanine → tyrosine	(*25*)
HeLa clones	Varying concentrations of serum protein		(*33*)
Small populations of HeLa cells (S3)	"Nonessential" amino acids (notably serine) required for optimum growth		(*34*)

on the order of 0.1m*M*, most of the nutritionally essential amino acids are concentrated by the cell approximately five- to tenfold. The degree to which the amino acid can be concentrated by the cell does, however, vary with the environment—from, for example, as much as 200-fold at an outside concentration of 0.001m*M* to as little as twofold at an outside concentration of 10m*M* (*26*). The rate of transport into the cell is quite rapid, usually reaching 75 percent of the equilibrium value within 15 minutes, and the loss of amino acid when the cells are placed in an amino-acid-deficient environment is correspondingly rapid.

It has been possible to determine for a number of specific amino acids the average intracellular concentration necessary for the initiation of protein synthesis and cell growth (*17*). When the pool concentration of a given amino acid was less than 0.01m*M*, there was usually no net synthesis of protein or cellular multiplication; maximum rates of protein synthesis and cell growth were observed at pool concentrations of 0.1 to 0.2m*M*, and at intermediate levels the rate of cellular growth varied directly with the amino acid concentration.

Metabolism of the Essential Amino Acids

All but one of the nutritionally essential amino acids so far studied (phenylalanine, tyrosine, lysine, valine, and threonine) have been found to be metabolized by the cell to only a minimal degree. Their primary function in cell cultures appears to be their utilization for incorporation into protein (*25, 35*). Glutamine, however, is actively metabolized. Over and above its direct utilization for protein synthesis, it is converted to glutamic acid, aspartic acid, asparagine, and proline and, to a limited degree, to serine and alanine as well. Its carbon skeleton is heavily used in the biosynthesis of pyrimidines, presumably by way of aspartic acid, and in the biosynthesis of both purines and pyrimidines, the glutamide amide nitrogen contributes more than half of the total base nitrogen (*28*). Its role in poliovirus synthesis is discussed below.

Protein Turnover

When cultures are overlaid with a medium lacking one or more essential amino acids, there is of course no net synthesis of protein. Isotopically labeled amino acids are nevertheless incorporated from such media into the cell protein at the surprisingly high rate of approximately 0.7 to 1 percent per hour (*25, 35*). This rate is uniform for all the cell lines and amino acids studied and may continue for as long as 72 hours, by which time more than 50 percent of the specific amino acid residues of the protein have been replaced. The reverse process (that is, the loss of amino acids from prelabeled cell protein) proceeds at the same rate, provided that the corresponding amino acid is present in the medium. This incorporation is largely an intracellular process and is only in small part due to either cell degeneration or protein secretion into the medium, followed by degradation to the amino acid level and resynthesis (*35*).

In animal cells, there is as yet no conclusive evidence as to whether this intracellular replacement of amino acid residues in cell protein involves the total breakdown of proteins to the amino acid level, followed by their resynthesis, or whether it is instead an exchange reaction between free amino acids in the cell pool and corresponding residues in an otherwise intact, or only partially degraded, protein molecule. Unlike the case in bacteria (*36*) and yeast (*37*), the turnover process occurs at essentially the same rate in growing as in nongrowing cultures, and is there evidenced by incorporation of a labeled amino acid into protein in amounts exceeding that represented by the new protein synthesized (*25, 35*). It is noteworthy that metabolic inhibitors such as azide, dinitrophenol, chloramphenicol, 6-mercaptopurine, and 5-fluorodeoxyuridine, at concentrations which totally inhibit the net synthesis of protein, have no significant effect on the rate of protein turnover (*17*).

Amino Acids in Biosynthesis of Poliovirus

In heavy monolayer cultures of the HeLa cell, the biosynthesis of poliovirus has been shown to require only glucose, glutamine, and salts (*38*); for the rest, the precursors for virus were derived from the cell itself. That study left open the question as to whether the viral protein was formed from the amino acid pool of the cell, whether the cells utilized their own protein for viral synthesis, or whether these two possibilities were the same, in the sense that cell protein turnover could supply the necessary free amino acids. Recent observations indicate that the synthesis of poliovirus by the HeLa cell requires the presence of a full complement of amino acids in the pool.

In contrast to the results obtained in large cell populations, when a relatively small number of cells were placed in a large volume of medium containing only glucose, glutamine, and salts, the amount of virus formed per cell was strikingly reduced (*39*). In this situation there is a rapid loss of amino acids from the cell pool (*17*); and the capacity of the cell to form virus was restored by the addition of a full complement of amino acids to the medium (*39*). It is clear that the optimal poliovirus synthesis by the HeLa cell requires the presence of free amino acids in the pool, and it is a reasonable presumption, borne out by recent experiments with labeled amino acids and purified virus (*40*), that these amino acids are used for the synthesis of viral protein.

It is of interest that the concentrations of glucose and of glutamine necessary for the optimal synthesis of virus were the same as those required for cell growth. Glutamic acid substituted for glutamine in virus propagation at the same high and nonphysiologic levels which permitted cell growth, and glutamic-adapted cells, which could grow at low levels of glutamic acid by virtue of their increased capacity to synthesize glutamine, formed maximal amounts of poliovirus at those same low levels (*41*).

General Considerations

Provision of the 28 essential metabolites outlined in Table 1, supplemented with serum protein, permits the large-scale cultivation of a wide variety of serially propagated cell lines in both monolayer and suspension cultures, at an average generation time in the logarithmic phase of growth of 18 to 24 hours. The same minimal medium, supplemented with serine, permits the growth of single human cells in 10 milliliters of culture fluid with 50 to 100 percent cloning efficiency. Some animal cell lines require further specific supplementation (see Table 4). Although this basal medium has been used successfully for the cultivation of cells directly from the animal host (*42*), there is no information as to the proportion of the cells which grow out, or as to the additional growth factors which would be required for maximally efficient cloning. Until such cloning can be achieved with essentially 100 percent efficiency, the identification of cell cultures as, for ex-

ample, "liver," "lung," or "bone marrow" is suspect. It is further to be noted that specialized organ functions are conspicuously absent in almost all serially propagated dispersed cell cultures. It remains to be determined whether this reflects incorrect identification of the cells, an irreversible loss of their biosynthetic capacities, absence from the environment of necessary precursors or cofactors, or the fact that cellular organization and interaction are essential to those specialized functions.

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Robert Emerson, Investigator of Photosynthesis

At the present state of knowledge of biology the experimental approach, designed to establish empirical relations between relevant variables, usually turns up unexpected effects and thus serves as the starting point for the development of entirely new concepts. Robert Emerson was particularly adept at this type of exploratory measurement uncommitted to any particular theory. His life was spent on experimental investigation of the mode of action of pigments in green plant photosynthesis. The effect of his career, directly on the field of photosynthesis and indirectly on related aspects of biology, is of particular value not only because of his own discoveries but also because he established unusually high standards of performance and critical self-evaluation of experimental measurements.

Born in 1903 to Haven Emerson (later to be public health commissioner for New York City as well as professor of public health at Columbia University) and a Philadelphia Quaker mother, he grew up in New York, attended the Ethical Culture School, and spent his summers in rural Long Island. He graduated from Harvard in 1925 and received his doctorate in 1927 from the University of Berlin; his work for the doctorate was based on studies of *Chlorella* respiration, made in collaboration with Otto Warburg. At this time he isolated the "Emerson strain" of *Chlorella pyrenoidosa*, which became the standard plant for photosynthesis research. He returned to Harvard for two years as a National Research Council fellow, and there he taught a course on photosynthesis and experimented with the effects of light intensity, temperature, and chlorophyll content on photosynthesis of *Chlorella*. In his lectures he made experimental data speak for themselves—a powerful technique that he developed to a high level of effectiveness.

In 1929 he married Claire Garrison and moved to California Institute of Technology. There, with the assistance of William Arnold, he investigated the effects of flashing light on photosynthesis. These experiments are the basis for the concept of the "photosynthetic unit"—a group of chlorophyll molecules functioning together as a single entity. This concept turned out to be very fruitful and continues to provide incentive for many new experiments and discussions.

Emerson's scientific work reflected his extraordinarily forceful character. Two characteristics that influenced the course of his research and left a vivid impression on his students and colleagues were his strong moral sense and his outrage at sloppy performance of any sort. His desire to do everything with excellence resulted in clear-cut, definitive scientific results. No relevant details of experi-

mentation were too minor to be set right, and his research was characterized by unusual care and thoughtful effort. He once made the comment that personal satisfaction in scientific research comes more from thorough and reliable work than from a larger output of lesser quality.

He enjoyed building things, particularly laboratory devices. The equipment he made was always solid, stable, and finished with a craftsmanship far beyond the ordinary in laboratory practice.

On leave from California Institute of Technology, he spent the years 1937 through 1940 as research associate in the Carnegie Institution's Division of Plant Biology, at Stanford, where he had the understanding support of Herman A. Spoehr. There, with the assistance of Charlton Lewis, he measured the effectiveness of different wavelengths of light for photosynthesis in *Chlorella* and *Chroococcus*. For this purpose they built an excellent grating monochromator with a high energy output. These measurements are basic to our present knowledge about participation in photosynthesis by the accessory pigments—carotenoids and phycobilins. Emerson and Lewis also discovered that light on the long-wave side of the red chlorophyll *a* absorption band is used very inefficiently. The carotenoids were found to be only partially effective, while the phycobilins contributed all their absorbed energy to photosynthesis.

Following up these experiments, Emerson and Lewis redetermined the efficiency of photosynthesis in *Chlorella* —a classical experiment of his former teacher, Otto Warburg, for whom he had deep admiration and respect. The results of the new measurements gave an efficiency about one-third to one-half the previous value of four quanta required to reduce a molecule of CO_2. This disagreement led to a long search for possible errors in both sets of measurements. Unfortunately, and quite unnecessarily, this disagreement developed into a bitter controversy, eventually involving several laboratories on both sides of the question. For Emerson it became a moral crusade of truth against error.

In 1946, after six more years at the California Institute of Technology, he was appointed research professor of botany at the University of Illinois, where he remained. There he and Eugene Rabinowitch developed a leading center of photosynthesis study. The quantum-yield crusade continued for many difficult years until it was established to his

Robert Emerson

own satisfaction that the results he obtained were incontestable. He then published a series of articles written with remarkable detachment from the controversy. He made it possible for Otto Warburg to come as a visiting professor to Urbana in order that the discrepancies could be amicably settled. At the present time each of the opposing groups of investigators considers the problem satisfactorily settled in their favor, which means that they still disagree as strongly as ever about the efficiency of photosynthesis.

Emerson's last years were the most productive of all as he again took up the mode of action of the different plant pigments concerned with photosynthesis. The low efficiency of long-wavelength red light previously discovered with Lewis had been on his mind during the intervening years. It had remained a puzzle whose solution he instinctively felt would mean important progress in understanding that step of the photosynthetic process in which the conversion of light to chemical energy takes place. He returned to this problem with the discovery that the efficiency of long-wave red light can be dramatically raised by simultaneous irradiation at shorter wavelengths. The stimulating effect of simultaneous light activation of other pigments as well as of chlorophyll *a* on photosynthesis was the subject of his work at the time of his death [R. Emerson and R. V. Chalmers, *Phycol Soc. Am. News Bull.* **11**, 51 (1959)]. These studies, of great current interest, have raised serious doubts about the concept that all photosynthetic pigments of plants act only by transferring their energy to chlorophyll *a*.

A remark which circulated among his friends was: "Bob considers the world a moral gymnasium in which he is at liberty to exercise his conscience daily." He was active in civil liberties organizations and was particularly concerned about discrimination against minority groups. The imprisonment of the American citizens of Japanese ancestry during World War II aroused his moral indignation. He worked hard to reduce the suffering of these people, both on the personal level and in educating government officials to pursue a more civilized policy. His professional knowledge of plant physiology and his friendship with highly skilled Japanese gardeners and technicians contributed to his effectiveness in a guayule culture research program for rubber production during the war.

He was a practising follower of his philosopher great uncle's cult of "plain living and high thinking." He raised his own chickens and vegetables, enjoyed homemade bread, shaved with an old-fashioned straight razor, and for relaxation made wood carvings.

In spite of his well-known scientific achievements and of honors such as the Stephen Hales award of the American Society of Plant Physiologists, the 50th Anniversary award of the American Botanical Society, and membership in the National Academy of Sciences, he never seemed to be aware of his high status, both as a scientist and as a man, nor did he ever seem to realize how greatly he was esteemed by everyone who either worked with him or argued against him.

Before World War II Emerson belonged to the small group of scientists who had chosen photosynthesis as their main scientific problem. Ten years later, after research with radioactive tracer carbon had become fashionable, the number of people working on photosynthesis expanded rapidly, and the number of published papers in this field has grown accordingly. But Emerson's death in an airplane accident at La Guardia field on 3 February 1959 suddenly makes us aware that there are still only a very few scientists in the entire world capable of approaching the core of the problem with his technical ingenuity, his special knowledge, and the extraordinary care he took to ensure the reliability of the data that he published.

C. Stacy French

Department of Plant Biology, Carnegie Institution of Washington, Stanford, California

News of Science

Industrial Security Program Invalidated by Supreme Court; New Legislation Studied

The Supreme Court invalidated the government's industrial security program, which covers some 3 million defense plant workers, including many scientists, when it held on 29 June that neither Congress nor the President had authorized a program in which suspects were denied the right to confront their accusers. The Court said that there had only been acquiescence, " 'inferred' authorization," by the President and Congress to the procedure that has been established by the Secretary of Defense and his service secretaries. The Court indicated, further, that the Secretary of Defense would not need additional authorization to organize a security program if he provided "the safeguards of confrontation and cross-examination."

The 8 to 1 decision was handed down in the case of William L. Greene, aeronautical engineer and former vice president of the Engineering and Research Corporation (ERCO), Riverdale, Md., whose security clearance was revoked by the Navy in 1953, although earlier he had been cleared on three different occasions. Since ERCO conducts classified defense work, Greene had to be dismissed. One of the firm's principal contracts is for a Navy aircraft flight simulator designed chiefly by Greene, who served the company for 18 years.

The Charges

In April 1954, a year after revocation of Greene's clearance, the Eastern Industrial Personnel Security Board finally presented a statement of charges, all based on incidents that occurred between 1942 and 1947, and granted a hearing. Most of the charges concerned Greene's ex-wife, from whom he had been divorced in 1947, primarily because of problems arising from political differences. He was accused of having associated with certain suspect persons (his wife and her friends); of having joined a bookshop group of questionable loyalty; of having attended a dinner given by the Southern Conference for Human Welfare, later cited as a Communist front organization—a dinner, incidentally, which was attended by many Washington notables, including members of the Supreme Court; and of having associated with officials of the Russian Embassy. In connection with this last charge, high-ranking ERCO officials testified that these contacts were for the purpose of securing business for the corporation.

The 1954 hearing began with a statement by the chairman that the transcript would not include all the material in the file of the case. During the course of the proceedings, the introduction of new subjects of inquiry by the government made it evident that the board was relying on reports from confidential informants. When his appeal was rejected, Greene asked for a detailed statement of findings in support of the decision. He was informed that security considerations prohibited such disclosure. His only recourse was the courts, where he held that he was being deprived of liberty and property without due process of law—"property" being his employment, and "liberty" his freedom to practice his profession. Greene had been earning a salary of $18,000 a year at ERCO, but he was forced to accept a $4400 post as an architectural draftsman.

Warren Writes Opinion

Chief Justice Earl Warren wrote the Court's opinion for the case, in which he was joined by Justices Hugo L. Black, William O. Douglas, William J. Brennan, Jr., and Potter Stewart. Warren said in part:

"Certain principles have remained relatively immutable in our jurisprudence. One of these is that where governmental action seriously injures an individual, and the reasonableness of the action depends on fact findings, the evidence used to prove the Government's case must be disclosed to the individual so that he has an opportunity to show that it is untrue. While this is important in the case of documentary evidence, it is even more important where the evidence consists of the testimony of individuals whose memory might be faulty or who, in fact, might be perjurers or persons motivated by malice, vindictiveness, intolerance, prejudice, or jealousy. We have formalized these protections in the requirements of confrontation and cross-examination. They have ancient roots. They find expression in the Sixth Amendment which provides that in all criminal cases the accused shall enjoy the right 'to be confronted with the witnesses against him.' This Court has been zealous to protect these rights from erosion. . . .

"Under the present clearance procedures not only is the testimony of absent witnesses allowed to stand without the probing questions of the person under attack which often uncover inconsistencies, lapses of recollection, and bias, but, in addition, even the members of the clearance boards do not see the informants or know their identities, but normally rely on an investigator's summary report of what the informant said without even examining the investigator personally. . . .

"In the instant case, petitioner's work opportunities have been severely limited on the basis of a fact determination rendered after a hearing which failed to comport with our traditional ideas of fair procedure. The type of hearing was the product of administrative decision not explicitly authorized by either Congress or the President. Whether those procedures under the circumstances comport with the Constitution we do not decide. Nor do we decide whether the President has inherent authority to create such a program, whether congressional action is necessary, or what the limits on executive or legislative authority may be. We decide only that in the absence of explicit authorization from either the President or Congress the respondents were not empowered to deprive petitioner of his job in a proceeding in which he was not afforded the safeguards of confrontation and cross-examination."

Justice Felix Frankfurter wrote a one-sentence concurrence, in which he was joined by Justices John Marshall Harlan and Charles Evans Whittaker, agreeing with the Chief Justice "that it has not been shown that either Congress or the President authorized the procedures whereby petitioner's security clearance

was revoked, [but] intimating no views as to the validity of those procedures." In a separate, special concurrence Harlan amplified his statement by saying he could not subscribe to the Court's opinion because it "unnecessarily deals with the very issue it disclaims deciding." Although Warren had stated that the Court did not need to decide the constitutional question of the right of confrontation, he devoted five pages to discussing it, starting with the Roman law of 2000 years ago.

Clark Dissents

Justice Tom Clark, in a lone dissent, observed:

"Surely one does not have a constitutional right to have access to the Government's military secrets. . . . What for anyone else would be considered a privilege at best has for Greene been enshrouded in constitutional protection. This sleight of hand is too much for me." In his special concurrence Harlan took sharp issue with this view and commented: "It is regrettable that my brother Clark should have so far yielded to the temptations of colorful characterization. . . ."

Clark emphasized that the Court's opinion, by dealing so "copiously" with the constitutional issues, had "put a cloud" over the entire federal employe loyalty program:

"While the Court disclaims deciding this constitutional question, no one reading the opinion will doubt that the explicit language of its broad sweep speaks in prophecy. Let us hope that the winds may change. If they do not the present temporary debacle will turn into a rout of our internal security."

Hearings Held

On 2 July, 3 days after the decision on the Greene case, the Senate Constitutional Rights Subcommittee, under the chairmanship of Senator Thomas C. Hennings, Jr., (D-Mo.), held a public hearing on methods of providing fair hearing procedures in federal loyalty-security programs, with particular reference to the industrial personnel security review program. One of the witnesses was Ralph S. Brown, Jr., professor of law at the Yale University School of Law and author of the recently published book *Loyalty and Security*.

He pointed out that confrontation and cross-examination are not the only elements of due process that are often ignored in security cases. He then mentioned four other defects, saying:

"First, the . . . alleged need for concealing the sources of derogatory information leads to inadequate charges, so that the employee does not know what he has to defend against. Second, in the hearings additional matters are often raised which have no relevance to the charges, or for that matter to the criteria of the programs. . . . Third, the findings on which decision is based, in the few instances in which they are disclosed, tend to stray from the charges, especially in raising questions of veracity of which the employee has been given no notice. Fourth, though the employee may have, under the regulations, a right of review or appeal to a higher authority than the hearing board, he will usually not be told what the findings are that are being reviewed and therefore cannot appeal intelligently. The Greene case itself demonstrates both of these deviations from fair procedure."

Another witness was Joseph Rauh, prominent Washington attorney and expert on civil liberties cases. He made some particularly constructive comments about the secret informer issue. After pointing out that throughout its history the United States Government had always employed undercover agents, Rauh observed: "I am not against undercover agents. The question is, how you use them. . . . We suggest that you use undercover agents in this field of security as you use them in every other field, as leads to get witnesses who will testify on the open record."

Recently, on 31 July, Senator Hennings announced that he had scheduled additional loyalty-security hearings on 28 and 29 July to which he had invited the Attorney General and the Secretary of Defense. However, both men refused to attend, indicating that the Administration had not yet formulated a position on the subject.

Hennings said that he was disturbed by reports that, as a result of the Greene decision, the Administration is considering the immediate issuance of an Executive Order covering hearing procedures under the industrial security program. He commented:

"I think it is highly important, before either Congress or the Administration acts in this matter, that the constitutional issues be explored carefully and thoroughly. . . . Since the Constitutional Rights Subcommittee is in the middle of a study of fair hearing procedures under the federal loyalty-security program, I do not think action should be taken until this study has been completed."

New Bills Offered

Meanwhile, four new loyalty-security bills have already been offered—one in the House and three in the Senate. Senator Hennings reports that he is preparing a fifth. [These are in addition to H.R. 3693 (Scherer), S.776 (Butler), and S.1916 (Cotton-Stennis), which have been pending since early spring.] The bill before the House is H.R. 8121, introduced by Francis E. Walter (D-Pa.). The Senate has before it S.2314, sponsored by Strom Thurmond (D-S.C.); S. 2392, sponsored by Owen D. Johnston (D-S.C.) and James O. Eastland (D-Miss.); and S. 2416, sponsored by Thomas J. Dodd (D-Conn.) and Kenneth B. Keating (R-N.Y.). The 29-page Thurmond bill provides that regularly established confidential informants shall be protected if the investigative agency concerned determines that the "disclosure of their identity would prejudice the national security." The Johnston-Eastland bill merely authorizes the continuation of the present program, as does the Walter bill in the House. The Dodd-Keating bill, brief and rather vague, provides that the right of confrontation be limited only in cases in which such confrontation or disclosure of a witness' activities would "adversely affect the national security, safety, or public interest." All of the Senate bills are being referred to the Internal Security Subcommittee. The Congress now has an opportunity to establish the structure for a personnel security program that will give consideration both to the legitimate needs of national security and to the requirements of due process.

Top-Level Decision Making in Science and Other Fields To Be Studied by Senate Group

A study of top-level governmental decision making in scientific, educational, and other fields is currently under way in Washington. The Senate's new National Policy Machinery subcommittee, headed by Henry M. Jackson (D-Wash.), will examine the policy-making procedures employed by the government in deciding issues of basic national and international significance. Among the questions that the group will ask are these: Was top-level consideration given to the psychological impact of permitting the Soviet Union to achieve scientific firsts in the missile and satellite field? Is such consideration being

given to the relationship between our present output of scientists and engineers and our future needs for these personnel? How extensive a military commitment will national resources permit?

The committee will study the ways in which these and other fundamental issues are decided and will suggest improvements, including, possibly, the creation of an academy of national policy similar in function to the National Academy of Sciences. President Eisenhower, reversing an earlier position, has assured Jackson of the cooperation of the executive office and of the National Security Council, the policy-making group that was the particular subject of a speech Jackson gave at the War College last April in which he outlined the weaknesses in the government's present executive organization.

Jackson and Senators Humphrey (D-Minn.) and Mundt (R-S.D.) are conducting the study because of their concern with the demands the East-West conflict makes on the institutions of a democracy. Jackson feels some of these institutions, those relating to policy making, must be evaluated in light of the new demands. One of the major factors that will decide the outcome of the conflict, Jackson believes, is the degree to which our government is able to present to the decision makers of the country clear alternatives on the issues the cold war is constantly bringing to the fore. The committee will concern itself only with the most basic decisions, made at the highest levels of government. An example from the past is the World War II decision to defeat Germany first and Japan second. Current examples of such questions, in addition to those bearing on science, are these: Should the increase of our gross national product be set as a goal of national policy? How much consideration has been given to the use of nuclear weapons in limited war?

Current Practices

Fundamental issues that bear on the eventual outcome of the cold war, Jackson maintains, are currently either not reaching top decision-making bodies such as the National Security Council or are reaching them in the form of fuzzy sets of alternatives or predecided recommendations. Such recommendations, Jackson suggests, are the result of low-level compromises among various departments of government. He believes that "plans which do not lead to sharp disputes at the NSC level are not good

Henry M. Jackson, who heads a new Senate committee which will examine U.S. policy-making procedures.

plans; they do not present the kind of issues which the top level ought to be called on to decide in this hard slugging contest between the Sino-Soviet bloc and ourselves. There is," he says, "a role for both Chiefs and Indians, and only confusion can result when the Indians try to do the work of compromise which is the job of the Chiefs."

Present practices, Jackson maintains, lead to confusion and ambiguity about national goals among both government leaders and the public. Today, when survival is the issue, we lack a "coherent and purposeful national program that sets forth in simple terms what we have to do to survive, and why." "In wartime," Jackson told his War College audience, "our leaders know, and our people know, what they are trying to do, and what is demanded of them. This makes possible the marvelous unity and energy of wartime. We have no comparable strategy for the cold war. Our leaders do not know, and the people surely do not know, what our purposes are and how we propose to achieve them. . . . Our people are never told what is required of them. The Congress is presented with only bits and pieces of policies—that give us no clear idea of what the Executive branch is really trying to accomplish."

Some Early Proposals

The failures and weaknesses of current policy-making procedures can be remedied, Jackson believes, by instituting a number of organizational changes. Some of these he suggested to the War College audience. Policy-planning staffs could be set up in each main department, with a position, role, and prestige like those of the Policy Planning Staff set up in the State Department during the Truman Administration. A policy committee could be organized in the form of an academy of national policy, outside the government but with access to classified information. The academy could draw on experts in national defense and in the sciences, social sciences, and humanities, and on leaders from public life. To the greatest extent possible the academy's reports would be made public, as part of a continuing effort to develop an informed public opinion. In addition, the academy would prepare confidential reports for use by the government. Unlike temporary committees, this center, being permanent, could build up a reputation for producing responsible and helpful reports. In the area of national scientific activities, the National Academy of Sciences has a similar role.

Other suggestions made by Jackson include redefinition of the National Security Council's role as that of identifying and clarifying policy choices for the President and his principal advisers. Its function would be that of sharpening policy choices in order to help the President and the National Science Council see the issues clearly and thus decide them intelligently.

Guidelines Adopted

Jackson's group, which is a subcommittee of the Senate's Committee on Government Organization, plans to study, rather than to investigate, current policy-making practices. In correspondence with the President it was agreed that the committee would be apolitical, and that there would be no sensationalism or attempts to embarrass officials. After a set of proposed guidelines had been adopted, the President assigned Charles A. Haskins, senior staff member of the Natonal Security Council, to work with the subcommittee. A professional staff for the group has been assembled; it includes at least two former members of the State Department's Policy Planning Staff.

Jackson, who at the age of 47 is starting his second term in the Senate, is generally regarded as a responsible and informed Senator with extensive experience on committees dealing with atomic energy, the armed services, and missile development. With his staff set up, and with the assurances of the President behind him, he has already begun work on his study of the government's policy-making machinery. In voting its unani-

mous approval of the study, the Senate allocated $60,000 and gave the committee until the end of January 1960 to complete its report. More money and an extension of time to June or July of next year will probably be requested by the subcommittee.

Jackson's group will work with representatives of the National Security Council in conducting the study. The issue, the men, and the cooperation of the President, observers suggest, indicate that the committee's work will lead to important legislation.

"Most Scientific" Satellite Put in Orbit 7 August

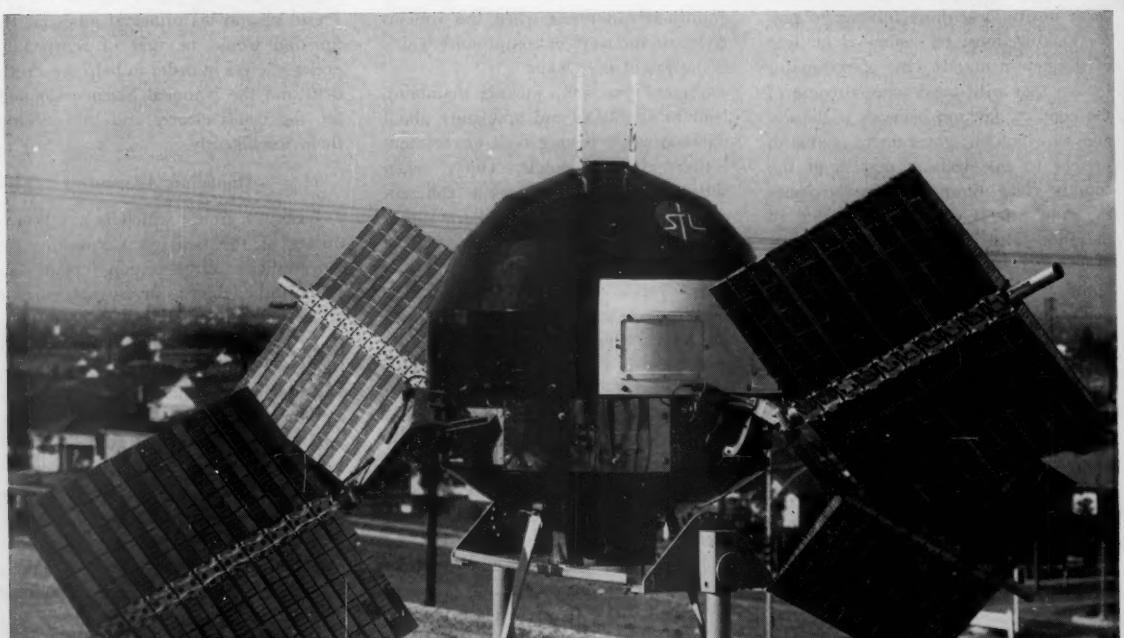
A 142-pound satellite, designed to conduct 15 experiments during its year of life, has been placed in a highly elliptical orbit around the earth by the National Aeronautics and Space Administration. The launching vehicle, a three-stage Thor-Able rocket, left the pad at Cape Canaveral at 10:23 A.M. on 7 August after one short delay in the countdown.

The satellite, which has an apogee of 26,400 miles and a perigee of 156, has the following devices and experiments: three devices to map the radiation belt ringing the earth with each of the instruments concentrating on a specific radiation energy level; a 2½-pound scanning device which is designed to relay a crude picture of the earth's cloud cover; 8000 solar cells, 1000 on each side of the four vanes, to generate current to recharge the satellite's chemical batteries; a micrometeorite detector to gauge the size and speed of meteoric particles hitting the satellite; two types of magnetometers to map the earth's magnetic field; and four experiments to study the behavior of radio waves, all aimed at finding out more about deep space communications. According to a NASA spokesman, all of the devices in the satellite were operating properly 3 days after the launching. Because of the four vanes, or "paddle wheels," projecting from its body, the new satellite is unusual in appearance.

Second Bill to Spur Private Philanthropy Given No More Chance than the First

A proposal to stimulate private philanthropy for education, embodying ideas recently put forth by Clifford C. Furnas, chancellor of the University of Buffalo, has been introduced in the House of Representatives. This is the second measure with this aim now before Congress. Earlier this year, Representative Frank Thompson, Jr., (D-N.J.) and Senator James E. Murray (D-Mont.) introduced identical bills providing all taxpayers with the same tax benefits for philanthropy that are now allowed persons in the top-income brackets. These bills, which reflected the conclusions of the AAAS-sponsored study "Stimulating Voluntary Giving to Higher Education and Other Programs," are before the House Ways and Means Committee and the Senate Finance Committee.

The new measure, which was introduced 23 July by Representative Harris B. McDowell, Jr., (D-Del.), allows $1 of



Payload of the Explorer VI rocket, launched 7 August from Cape Canaveral by the National Aeronautics and Space Administration. The satellite, which weighs 142 pounds, is shown with solar cell paddle wheels extended. The launching vehicle was a Thor-Able rocket.

tax credit for every $1 given to institutions of higher learning by individuals and corporations. In the case of an individual, this credit would be limited to 10 percent of his adjusted gross income if he takes the standard deduction or uses the short form for his tax return, or 30 percent if he itemizes his deductions; in the case of a corporation the limit would be 5 percent of taxable income. Within these limits it would, in effect, cost the taxpayer nothing to contribute to education. Chancellor Furnas estimates that a plan such as that proposed by Congressman McDowell will yield approximately $2 billion for higher education.

Under provisions of the bills introduced earlier this year by Thompson and Murray, the flow of funds to education would be increased by allowing all taxpayers to subtract from their tax payments 91 percent (52 percent for corporations) of the amount they had contributed to institutions of higher education within an upper limit of 15 percent (10 percent for corporations) of their adjusted gross income.

Administration Opposed

Reports on the bills from the governmental departments will almost without question be unfavorable. Previously proposed legislation, particularly that concerned with tax credits for college tuition, has revealed the Administration's position on such measures. The Department of Health, Education, and Welfare has opposed such tax credit measures on the grounds that they are inconsistent with good public policy. In the department's view, support of bills such as the McDowell and Thompson proposals would constitute an abdication of responsibility. Public funds, the department feels, should be disbursed by the elected representatives of the people—the Congress—on the basis of criteria set up to meet the educational needs of the country as a whole. Otherwise, in the administration's view, there would be no guarantee that particularly needy educational institutions would receive the support they require. Tax revenues that are now being used to support such nationwide programs as that set up through the National Defense Educational Act would, the department feels, be donated to institutions preferred by the individual taxpayer.

The Treasury Department opposes tax credit bills of this type on the simple grounds that they deprive the federal government of funds due it under present income tax laws. If, as Furnas suggests, a bill based on his proposals will bring in $2 billion to educational institutions, it will also divert that much revenue from the government.

Opposition on these grounds, which apply equally to the McDowell and Thompson bills, will probably result in strongly unfavorable reports from the departments. How will these reports influence the two committees to which the bills have been referred? To judge from past response to measures of this nature, only a heavy and concerted drive in Congress could make the current bills into law. There is little evidence that such a drive is in preparation.

Committees Named for Science Writing Awards

Ten represenatives from the fields of journalism, science, and education have been named to administer the recently established AAAS-Westinghouse Science Writing Awards. The ten, who will compose the screening and judging committees, will select the best science writing, exclusive of that in medicine, to appear in the nation's newspapers and general magazines during the current contest year. The writer of the best science story in each of the two types of publications will be awarded $1000. The awards will be presented at the annual meeting of the AAAS in Chicago in December.

The judges are: Graham DuShane, editor of *Science*; Earl English, dean of the school of journalism at the University of Missouri; Caryl Haskins, president of the Carnegie Institution of Washington; James A. Linen, publisher of *Time*; Morris Meister, president of Bronx Community College; Alan T. Waterman, director of the National Science Foundation; and J. Russell Wiggins, vice president and executive editor, *Washington Post and Times Herald*, and president of the American Society of Newspaper Editors.

The screening committe has the following members: Hillier Kriegbaum, department of journalism, New York University; Sidney Negus, department of biochemistry, Medical College of Virginia; and James Stokley, school of journalism, Michigan State University.

The AAAS-Westinghouse Science Writing Awards were established to give recognition and encouragement to outstanding science writing, to stimulate public interest in science, and to foster a deeper understanding of the significance of science by the general public. The AAAS, the National Association of Science Writers, and Westinghouse cooperated in setting up the awards, which are supported by a grant from the Westinghouse Educational Foundation.

Entries in the newspaper competition must have been published between 1 October 1958 and 30 September 1959; in the magazine competition, entries must have appeared in editions dated between October 1958 and September 1959 inclusive. To be eligible, all entries must be posted before midnight, 10 October 1959, and must have been published in a newspaper or magazine within the United States.

Inquiries about the competition and requests for entry blanks by entrants or their editors should be addressed to: Graham DuShane, Administrator, AAAS-Westinghouse Science Writing Awards, 1515 Massachusetts Ave., NW, Washington 5, D.C.

"Takuyo Maru," Another "Lucky Dragon"?

Last July the Japanese Coast Guard vessel *Takuyo Maru* abandoned a scientific survey in the South Pacific after encountering radioactive rain 186 miles outside the danger zone for the United States Eniwetok nuclear test area. Now Hirokicho Nagano, 34, chief engineer of the survey ship, has died of leukemia. The Associated Press quotes Japanese officials as having said on 5 August:

"We cannot announce the cause of death now because it is a very delicate matter that could cause international repercussions. There will be an announcement later."

A spokesman for the Atomic Energy Commission reports that the medical question of whether or not the leukemia can be traced to the incident is under investigation. At the time of the accident, American and Japanese physicians examined the crew and found no evidence of harmful radiation, although some of the men had suffered a decrease in white blood corpuscles. Nagano was one of these.

There have been no continuing medical studies because the levels of exposure were considered to have been very low. However, a definite figure is not available since the *Takuyo Maru* did not carry instruments for measuring radioactivity. In fact, last summer Japanese newspapers were sharply critical because the vessel had been sent into the area without a Geiger counter.

Nagano's death may well grow into

an international issue such as that precipitated by the death in 1954 of Aikichi Kuboyama, one of 23 men aboard the Japanese fishing boat *Lucky Dragon*, which was dusted with radioactive fallout from a United States nuclear test at Bikini. In compensation, the United States paid Japan $2 million.

The impact of the current incident is intensified by the timing, for announcement of the death came just before the anniversary on 6 August of the atomic bombing of Hiroshima, which killed at least 100,000 people. Now, 14 years later, 90,000 are still under medical care. The tragic moment, 8:15 A.M., is marked in Hiroshima by tolling bells and a mass meeting at a memorial built in an area known as Ground Zero. This year, as in others, the bells also signify the opening of the World Convention Against Nuclear Weapons, attended by delegates from all over the world.

Radiation in Industry

An international conference will convene in Warsaw, Poland, on 8 September to discuss the application of large radiation sources in industry, particularly in industrial chemical processes. The meeting, which is being organized by the International Atomic Energy Agency, will last 5 days and will be attended by more than 200 delegates from all parts of the world. This will be the first major scientific conference to be held by the agency to promote the peaceful use of nuclear radiation.

The U.S. Atomic Energy Commission has announced that the Oak Ridge Institute of Nuclear Studies is coordinating U.S. participation. A committee set up by ORINS recommended papers for oral presentation; however, all abstracts were transmitted to the IAEA, which made the final selection. Approximately 20 papers from the U.S. will be read.

Scientists in the News

Colonel FRANK M. TOWNSEND, the senior pathologist of the U.S. Air Force, has been appointed director of the Armed Forces Institute of Pathology, Washington, D.C. He succeeds Captain WILLIAM M. SILLIPHANT, M.C., U.S. Navy.

RONALD SINGER, professor of anatomy at the University of Capetown, Union of South Africa, will serve for a year as visiting associate professor in the department of anatomy at the University of Illinois College of Medicine. He succeeds C. W. M. PRATT, lecturer in anatomy at Cambridge University, England, who has returned home after a year's stay. Singer is serving at Illinois in the absence of JAMES C. PLAGGE, who is completing his second year with the International Cooperation Administration as a medical educator in Saigon, Vietnam.

JOHN P. GILLIN, professor of anthropology and research at the University of North Carolina, has been appointed dean of the Divison of Social Sciences and professor of anthropology at the University of Pittsburgh, effective 1 September.

HENRY E. BENT, dean of the graduate faculty and professor of chemistry at the University of Missouri, will head the graduate fellowship program of the National Defense Education Act, effective in September. The graduate fellowship program is designed to increase the number of college teachers and to expand and promote wider geographical distribution of graduate-school facilities.

ROBERT PERLOFF, director of research and development at Science Research Associates, Inc., Chicago, Ill., has been appointed associate professor of psychology at Purdue University.

NORMAN H. RICKER, formerly senior research physicist at Carter Oil Company, Tulsa, Okla., has been appointed professor of physics at the University of Oklahoma, Norman.

NORMAN H. SULKIN, professor of anatomy and acting chairman of the department of anatomy at the Bowman Gray School of Medicine, Wake Forest College, Winston-Salem, N.C., has been appointed chairman of that department.

ARNOLD A. ZIMMERMANN, professor of anatomy at the University of Illinois College of Medicine, will retire on 1 September as professor emeritus. A noted embryologist and anatomist, he received his D.Sc. in Geneva, Switzerland, in 1921. He had been affiliated with the Hooper Foundation in California, the Mayo Clinic, and the Loyola College of Medicine in Chicago before joining the University of Illinois in 1929. His research has included studies on the embryology of the lymphatic system, the comparative anatomy of vascular systems, developmental cardiac anomalies, and the development of the rattle in rattlesnakes. Zimmermann will continue to teach, in the department of anatomy at Baylor University Medical School and at the University of Texas Dental Branch in Houston, Tex.

HILARY KOPROWSKI, professor of research medicine at the University of Pennsylvania, has been awarded the 1959 Alvarenga Prize of the College of Physicians of Philadelphia for his research on the development of a living attenuated virus vaccine against poliomyelitis.

JOSEPH H. BURCKHALTER, head of the department of pharmaceutical chemistry at the University of Kansas School of Pharmacy, has been appointed professor of pharmaceutical chemistry at the University of Michigan's College of Pharmacy, effective September 1960. He will succeed F. F. BLICKE, who will retire on 30 June 1960.

JACOB L. GEWIRTZ, psychologist with the Laboratory of Psychology, National Institute of Mental Health, Bethesda, Md., will be on leave of absence, beginning 1 October, to serve as visiting professor of psychology at the Hebrew University, Jerusalem, Israel.

BLUE A. CARSTENSON, training consultant to the California State Hospital, Stockton, and the California Department of Mental Hygiene, has been appointed specialist for education on aging in the Office of Education, U.S. Department of Health, Education, and Welfare, Washington, D.C. He will also serve as technical director for the education panel of the White House Conference on Aging.

JACOB H. CONN, practicing psychiatrist and assistant professor of psychiatry at the Johns Hopkins University Medical School, has been elected president of the National Society for Clinical and Experimental Hypnosis.

Colonel JOHN A. NORCROSS, U.S. Air Force, has been appointed industrial physician in the health protection branch of the Atomic Energy Commission's Division of Biology and Medicine.

STANLEY L. LEE, director of hematology at Maimonides Hospital, Brooklyn, N.Y., has been appointed associate professor of medicine at the State University of New York Downstate Medical Center, Brooklyn.

Book Reviews

Population and Progress in the Far East. Warren S. Thompson. University of Chicago Press, Chicago, Ill., 1959. 443 pp. $7.50.

In this book, Warren Thompson, the distinguished and well-known population expert, writes of Asian economic, sociocultural, and population problems with knowledge, understanding, and sympathy. In a sense, the book dates back to 1929 when Thompson brought out his prophetic *Danger Spots in World Population,* wherein he pointed out the relationship between population pressure and wars and pleaded for some understanding of the economic problems of overcrowded countries. In 1946 he undertook a revision of that book but brought out what was really a new book, *Population and Peace in the Pacific,* the first competent and objective demographic survey of the region. Now Thompson has revised this and written what is in many ways another new book, *Population and Progress in the Far East.*

The title is apt, for here the author notes and evaluates the remarkable political, cultural, economic, and social changes (and their interrelationship with basic demographic factors) that have occurred in the region since the termination of World War II. Today, except for a few minor areas, Asia is politically free and has overthrown the discredited and unwanted European imperialism. (The British quit voluntarily and gracefully; the Dutch and the French, not so gracefully.) Economically, Asia is undergoing belated agricultural and industrial revolutions. More land is being brought under cultivation, land which through the centuries has been considered second-rate and uncultivable. Production per unit under cultivation is increasing, through the use of modern agricultural techniques. Despite limitations of raw materials, capital resources, and technological "know-how," every country in the region has embarked on heavy and large-scale industrialization, thanks to the assistance of the United Nations and its specialized agencies, to economic aid from the United States, to the Colombo Plan, and to other assistance. The Asian countries hope that industrialization will help to siphon surplus population from overcrowded agricultural regions into urban manufacturing areas.

The emancipation of women has begun, and Asian women today occupy responsible positions and are gaining political, legal, and economic equality with men. What is more, Asia is trying to lift up the segments of its population which, through social and religious tradition, have been submerged and discriminated against. The hard cake of custom that offers resistance to change is being broken in Asia. Planned changes as well as involuntary changes in response to newly introduced technological innovations are taking place. Asia is trying to move from the bullock-cart stage to the jet age in one incredible leap.

Perhaps the most important change is in the economic-political structure of government and society. Every Asian country is witnessing a struggle between conflicting ideologies—between individual freedom, democracy and free enterprise, and all that is best in the Western liberal tradition on the one hand and totalitarianism, regimentation, "democratic dictatorship," and communization on the other. In the race for rapid economic development the conflict is symbolized by India and China—the one with its freedom, democracy, and mixed economy and the other with its Communist controls and regimentation.

Herein also lies the basic controversy between Malthus and Marx. Are huge populations an asset or a liability in an underdeveloped country attempting to raise its living standards? Japan and India are dedicated to an official policy of planned parenthood, whereas in China today the policy is pronatalist. Although for nearly 3 years the People's Republic of China embarked on a vigorous campaign for birth control, last year the policy was reversed in favor of the Marxian view of the population question. And if China's communist economy is able to deliver the goods despite her teeming numbers and her alarming rate of growth (the net annual increase today is more than 20 million), the people of India may begin to wonder why their numbers must be reduced to facilitate quick economic progress. On the other hand, China might use her massive numbers as an excuse for expansion in the near future.

Thompson covers all these problems and more, as they are seen in Japan, India, China, Pakistan, Ceylon, Burma, Thailand, Cambodia, North and South Vietnam, Korea, and Taiwan, and includes a wealth of documentary evidence and personal observation. His observations on the demographic situation in all these areas are sound and relevant. However, his picture of policy in China is no longer accurate, for the policy has been changed since the book went to press.

It is impossible in a brief review to do justice to Thompson's book. It should be compulsory reading for every student of Asian affairs, and not just for demographers or social scientists. Both the author and the publisher are to be congratulated on having given us this book.

S. CHANDRASEKHAR
Indian Institute for Population Studies, Madras, India

A Record of History and Evolution of Early American Bridges. Llewellyn Nathaniel Edwards. University Press, Orono, Maine. 1959. xii + 204 pp. Plates. $5.

Although Llewellyn Edwards maintained that his intensive studies of the history of American bridges were a hobby, this little book is anything but the work of an amateur. The completed manuscript was prepared for publication through the efforts of Edwards' widow and a number of his former colleagues. The resulting volume is a valuable addition to the literature on the development of bridge engineering—a subject that deserves fuller analytical treatment than has been given it in the past. There is certainly no lack of effusive writing on the architectural and scenic character of the bridge, but there is too little serious consideration of the technical significance of the bridge in terms of materials and structural theory.

As an active and successful bridge designer until shortly before his death

in 1952, Edwards was well qualified to undertake this project, and he was one of the few writers with the necessary background who have appeared in this field.

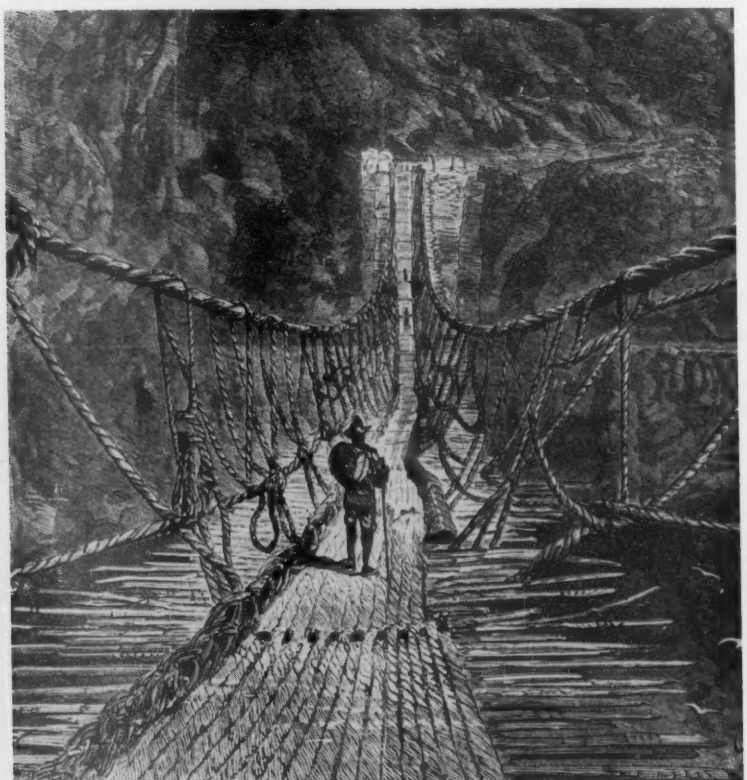
The work is divided into four periods —pre-Colonial, Colonial, post-Revolution, and post-Civil War—and this division reflects its organization as a survey of general development. This approach, which differs from the more conventional presentation, made either in terms of the materials used or by major structural systems, permits a clearer discussion of the complex relationships between the practical need for bridges, the current state of technology, the availability of materials, and the influence of tradition.

Several other aspects of the work are unusual and of very real value. One is the great amount of material that Edwards uncovered on American bridges built before and shortly after the Revolution, including several bridges in South America. Since they are, naturally, the least well documented, the bridges of this period have received only the most casual attention from historians, and information on fewer than half a dozen of them has been readily available until now. The inclusion of a number of unbuilt projects in the discussion is unique. The many freak proposals are not mentioned, only those which appear to have been rationally conceived, and plausible, if bold, for their time. Ellet's proposed iron suspension spans for St. Louis (1840) and Georgetown, Maryland (1852), receive a deserved amount of attention. A further interesting sidelight is the description of a little known, unbuilt, iron-bowstring truss designed in 1796 by the civil engineer Robert Fulton. Far from being of marginal value, information of this sort is as essential in a comprehensive study of the history of bridges as description of completed works.

It is regrettable that a need for economy in publishing the volume permitted the inclusion of only a small portion of the material resulting from the author's extensive and very competent research. This same restriction made it necessary to confine the illustrations to a single grouping at the end of the book—a disconcerting arrangement. Careful editing would have prevented the mismatching of two photographs with their captions and with the text.

These are insignificant faults compared to the major contribution Edwards made in a branch of technological history which has received so little serious attention.

ROBERT M. VOGEL
Smithsonian Institution, Washington, D.C.



Aboriginal bridge over Apurimac River, Peru. [From *A Record of History and Evolution of Early American Bridges*]

The Cellular Slime Molds. John Tyler Bonner. Princeton University Press, Princeton, N.J., 1959. viii + 150 pp. Illus. $4.

In his previous books, Bonner has displayed a charming gift for light treatment of biological problems. The present work, envisioned in the introduction as "a comprehensive survey of all the different known aspects of the biology of the cellular slime molds" and "a useful summary of all the work done before 1959," is a more scholarly undertaking. It is not nearly so successful.

My most general objection to this book is that, while Bonner takes decided stands in evaluating previous investigations, he does not provide enough factual information about experimental methods and results to enable readers to do their own evaluating. It is an astonishing fact that the 150 pages include one histogram, one semidiagrammatic graph, and no tables at all, to represent what is, by now, a considerable body of quantitative information about slime mold development, genetics, and physiology.

Despite the author's intention of providing a complete survey, a number of pertinent papers and experiments have been slighted. For example, the superb paper of Raper and Fennell on the construction of the fruiting body—which serves as a foundation of the modern description of culmination—is accorded a single short paragraph, on page 107, among pages of observations and considerations of much less import. The recent work of my coworkers and me on the identification of the initiator cell for slime mold aggregation is cited in a footnote on page 89 but is not described, and the experiments which showed a Poissonian distribution of aggregative centers among small population samples, as well as a large body of data concerning synergistic aggregation by cell mixtures of wild type and aggregateless mutants—work which provided the basis

for the initiator cell hypothesis—are not mentioned at all. Wilson and Ross' photomicrographic data, which suggest the possibility of meiosis, are mentioned briefly but are not pictured, and the chromosomal figures are not evaluated. Instead, on pages 39 and 40 Bonner belabors a very dead horse—the original scheme of sexuality that was proposed by Wilson and that died in 1957 by its creator's hand. As one of the pallbearers, I submit that the modified scheme of Wilson and Ross, summarily dismissed on page 41, deserves far more serious consideration than it is granted. Finally, Gregg's stimulating work on the appearance of surface antigens during morphogenesis is covered in a single short paragraph, on page 112, without inclusion of specific data.

In view of the paucity of detailed, quantitative information and the rather superficial treatment of underlying genetic and biochemical problems, this book does not seem to me to be an improvement upon the several reviews of the biology of the cellular slime molds that are now available.

MAURICE SUSSMAN
Department of Biological Sciences, Brandeis University

Exploration Hydrobiologique des Lacs Kivu, Édouard et Albert (1952–1954). Scientific results. vol. 3, fascicule 3. Institut Royal des Sciences Naturelles de Belgique, Brussels, 1959. 196 pp. Illus.

Among the most important of the reports on the fauna and flora of tropical areas published in recent years have been the several extensive series of volumes issued by the Institute of the National Parks of the Belgian Congo. Somewhat in the nature of a companion series are those issued by the Royal Institute of Natural Sciences of Belgium on the natural history of African areas which have been the subject of special Belgian explorations. The current reports on lakes Kivu, Edward, and Albert follow and are comparable to several volumes dealing with the 1946–1947 hydrobiological exploration of Lake Tanganyika.

The present fascicule contains six reports. The first of these, by Jean Verbeke of Brussels, deals with the stomach and intestinal contents of the fish of lakes Edward and Albert. In the brief introduction the relatively impoverished fish fauna of Lake Edward, consisting of 27 species, is compared to the fish fauna of Lake Albert, which includes 41 recorded species. There follow extensive lists and tables of the fish and of their food resources, based on many captures—of 17 and 23 species, respectively—from the two lakes. Details of place, time, condition, method of capture, and so on for each fish examined are well documented and are presented together with an enumeration of the stomach and intestinal contents identified. An ultimate practical objective of reports such as this is evidently the acquisition of sufficient information to make possible the improvement of the fish resources of these lakes, perhaps partly through the introduction of species which do not now occur.

The second paper, on Cladocera (water fleas), is by Vincent Brehm of Lunz am See, who has had over 45 years of experience with the group. It deals with the Cladocera of the three lakes, mainly those taken in and about the lakes but also those removed from fish. The discussion and tabulation concern 24 species, none of which is described as new, though the anatomy and specific characters of several are described and illustrated.

In the third paper, W. D. Hincks, of Manchester, reports briefly on 200 specimens of Dermaptera (earwings), representing 10 species. Except for two poorly known species of *Spongovostox*, those recorded are rather common, widely distributed species.

A rather full report on the Trichoptera (caddis flies) of Lake Albert, by Serge Jacquemart of Brussels, comprises the fourth paper. A total of 25 species are treated, the majority being illustrated; of the 25, three are described as new. About half of the species were not encountered at lakes Kivu and Edward, according to a report by Jacquemart in fascicule 2.

Larvae of Chironomidae (midges) of the three lakes are dealt with in detail by Anna Chrispeels of Edinburgh. Twenty-six species are treated, and all of them are illustrated, but specific names could not be applied with certainty to any of them. Generic or species-group placement must suffice until rearing of the larvae and association of the individuals with identified adults have been accomplished. The Chironomidae are one of the principal foods of the lake fishes, and this situation demonstrates the exacting and time-consuming biological and taxonomic work required for a full understanding of the insects comprising much of the diet of these important animals. The illustrations consist of fine, detailed line drawings, mainly of head structures and terminal portions of the abdomen. Descriptions, identification keys, documentation of collecting stations and material removed from fish, and a bibliography are included. Adult Chironomidae were discussed by P. Freeman in fascicule 2.

The sixth and final paper is a brief account of the Bostrychidae (false powder-post beetles) by J.-M. Vrydagh of Brussels. Sixteen species, in nine genera, of this family were collected near the three lakes. The author expresses the opinion that, while adults sometimes are attracted to light at night, it is a mistake to consider this a general habit.

ASHLEY B. GURNEY
Entomology Research Division, U.S. Department of Agriculture

Elements of Physical Metallurgy. Albert G. Guy. Addison-Wesley, Reading, Mass., ed. 2, 1959. xvi + 528 pp. Illus. $9.50.

Elements of Physical Metallurgy is a well-organized, well-written book on physical metallurgy. The author has fulfilled his objective of writing a book which can be used as a textbook for science, engineering, and metallurgy students. It should also prove a useful addition to the library of the practicing metallurgist, since it presents the fundamentals of physical metallurgy in a very readable manner and (in this second edition) covers the latest concepts of dislocation theory.

In the first two chapters, the field of metallurgy is defined and surveyed. In the next four chapters atomic theory, crystal structure, phases in metal systems, and phase diagrams are covered. In the latter chapters some industrially important equilibrium diagrams are discussed. With these chapters as a background, the author then discusses the physical properties, elasticity, plasticity, and corrosion (air, water, and liquid metal) of metals.

The last four chapters are concerned with reactions in metals: diffusion in metals; recovery, recrystallization, and grain growth; age hardening; and heat treatment of steels. The book is well illustrated, and each chapter concludes with a list of references as well as a number of problems. Throughout the book, the author shows how the basic principles are applied in industry.

This book covers a great deal of material and should make an excellent text

for a course in physical metallurgy. A few errors appear in the text. On page 45, in the illustrative problem, E equals 3.97×10^{-12}, not 3.97×10^{-22}; on page 66 it is stated that thorium is a nuclear fuel (it is actually a fertile material which can be converted by neutron absorption into a fuel); on page 77, in Fig. 4a, the Cs ion appears in the sodium chloride structure; and on page 184 the ends of the tie line at the base of Fig. 6–13 extend beyond the phases in equilibrium. Finally, the section on metals in nuclear engineering seems out of place at the end of chapter 3. In future editions this section should be amplified.

DAVID H. GURINSKY
General Atomic Division,
General Dynamics Corporation,
San Diego, California

A History of Western Technology. Friedrich Klemm. Translated by Dorothea Waley Singer. Scribner's, New York, 1959. 401 pp. Illus. + plates. $6.50.

This is a translation of a work originally published in Germany in 1954, in the series *Orbis Academicus, Histories of Scientific Problems in Documents and Descriptions.* The body of the book consists of selections from the sources, connected by the author's commentary. Such an approach to the history of technology seems never to have been tried before, and the author shows it to be surprisingly rewarding in this field, which is generally thought to be wanting in written records.

The author, who is librarian of the famous Deutsches Museum, shows himself to be steeped in the little-known literature of early technology. Not only has he quoted from such authors as the Italians Alberti, Martini, Filarete, and Fontana, and the Germans Glauber, Boeckler, Leupold, and Calvoer, but he has woven the quotations into what is surely the most readable history of technology yet published. If the German writers are favored, they are less favored here than they are neglected in most works on this subject.

As is usual in one-volume histories of technology (of which there are very few), the earlier periods are treated in a leisurely fashion, and later periods with increasing brevity, and the 20th century with a bare snapshot. Klemm's exposition of the Middle Ages and of the era that followed, through the 17th century, is outstanding, and as this is the darkest age of technology, this section gives his book its greatest distinction. Some of the source materials quoted are as thought-provoking as they are unusual. Examples are the Council Decrees of 16th-century Nürnberg in the matter of the inventive "red metal turner" Hans Spaichl, and the quoted impressions of European visitors to the Philadelphia Fair of 1876.

The translation is generally satisfactory, and it is gratifying to have this outstanding book rendered so promptly into English. It is very much to be regretted, however, that the publisher of the English edition saw fit to omit so much of the priceless accessory documentation contained in the German edition. The footnotes referring to sources and secondary works have been retained, but the bibliography has been reduced from ten pages to four (the reduction is actually greater than this would indicate, for the pages of the German editions are closely packed), through the elimination of all but English works. Omitted entirely from the English edition are a 6-page chronology of events in the history of technology and a 17-page bibliography of sources. Anyone seriously interested in further reading in the subject must, therefore, have recourse to the original.

ROBERT P. MULTHAUF
Department of Science and Technology,
Smithsonian Institution

New Books

Analytical and Canonical Formalism in Physics. André Mercier. North-Holland, Amsterdam; Interscience, New York, 1959. 229 pp. $6.75.

The Chemistry of Organic Compounds. A year's course in organic chemistry. James Bryant Conant and Albert Harold Blatt. Macmillan, New York, ed. 5, 1959. 660 pp. $7.75.

Ground Water Hydrology. David Keith Todd. Wiley, New York; Chapman & Hall, London, 1959. 348 pp. $10.75.

The Hand of Life. The story of the Weizmann Institute. Ritchie Calder. Weidenfeld and Nicolson, London, 1959. 78 pp. 30s.

Handbuch der Physik. vol. 41, pt. 1, *Nuclear Reactions 2: Theory,* 587 pp., DM. 145; vol. 44, *Nuclear Instrumentation* 1, 480 pp., DM. 125; vol. 53, *Astrophysics 4: Stellar Systems,* 573 pp., DM. 142. S. Flügge, Ed. Springer, Berlin, 1959.

High Temperature Materials. R. F. Hehemann and G. Mervin Ault, Eds. Wiley, New York; Chapman & Hall, London, 1959. 560 pp. $17.50. The papers in this volume are the results of the symposium on recent developments in high temperature materials that was held 16–17 April 1957 in Cleveland, Ohio. The symposium was sponsored by the Metallurgical Society and the American Institute of Mining, Metallurgical, and Petroleum Engineers. Thirty-four papers by 51 contributors are presented under the following general sections: "Cobalt- and nickel-base alloys," "Cermets and intermetallics," "Refractory metals," "Strengthening by dispersion of insoluble particles," "Vacuum melting and its effects on properties," "Effect of testing environment on properties," "Oxidation resistance."

Methods of Vegetation Study. Edwin Allen Phillips. Holt, New York, 1959. 107 pp. $2.95.

Microbiology, Yesterday and Today. Vernon Bryson, Ed. Inst. of Microbiology, Rutgers Univ., New Brunswick, N.J., 1959. 127 pp. $4. This volume consists of the proceedings of a symposium held at the institute on 5 June 1958 in honor of the 70th birthday of Selman A. Waksman. The contents of the volume are: "Microbial biochemistry and its development" (J. H. Quastel); "Antibiotics—a new field for microbiological research and perspectives for the future" (H. B. Woodruff); "Episodes in immunochemistry" (M. Heidelberger); "Bacterial classification—problems and developments" (S. T. Cowan); "Some contributions of genetics to microbiology" (V. Bryson); "Aspects of Russian microbiology" (G. K. Skriabin); "Microbiology yesterday and today" (S. A. Waksman).

National Tuberculosis Association, 1904–1955. Virginia Cameron and Esmond R. Long. National Tuberculosis Assoc., New York, 1959. 335 pp. $5.

Principles and Practice of Gas Chromatography. Robert L. Pecsok, Ed. Wiley, New York; Chapman & Hall, London, 1959. 238 pp. $6.75. This book is the result of a course in gas chromatography offered by the University of California in February 1959. The 13 chapters are based on lectures by C. M. Drew, S. A. Greene, H. S. Knight, and H. W. Patton.

Push and Pull. The story of energy. Paul Blackwood. McGraw-Hill, New York, 1959. 190 pp. $3 (juvenile book).

Recent Advances in the Chemistry of Cellulose and Starch. J. Honeyman, Ed. Interscience, New York, 1959. 366 pp. $9.25.

Subcellular Particles. A symposium. Teru Hayashi, Ed. Ronald, New York, 1959. 221 pp. $6.

Survey Adjustment and Least Squares. Hume F. Rainsford. Ungar, New York, 1958. 334 pp. $9.50.

Traité de Chimie Biologique. vol. 2, pt. 1, *Substances minérales—glucides*; pt. 2, *Vitamines, lipides, stérides, caroténoides, fermentations, photosynthèse.* Louis Genevois. Presses Universitaires de France, Paris, 1959. 880 pp. Paper, F. 2200.

Ultracentrifugation in Biochemistry. Howard K. Schachman. Academic Press, New York, 1959. 284 pp. $8.80.

The Viruses. Biochemical, biological, and biophysical properties. vol. 3, *Animal Viruses.* F. M. Burnet and W. M. Stanley, Eds. Academic Press, New York, 1959. 445 pp. $12.

Reports

Isolation of a Hemolytic Component of Fire Ant Venom

Abstract. A crystalline hemolytic principle, shown to be a constituent of fire ant venom and having the properties of an amine, was isolated from crude extracts of whole ants. The chromatographic procedure of isolation is described, and a preliminary report is given about some properties of the substance.

Interest in the responses to the sting of the fire ant (*Solenopsis saevissima*) and in its venom has been indicated in several recent publications (*1–3*). It has been reported that human subjects stung by fire ants show reactions of two types: a local necrosis and a systemic reaction presumably due to allergy (*1*). The present report (*4*) represents the first stage of our investigations of the nature of the necrotoxic principle(s) of the venom.

In studies (*3*) of some of the pharmacological properties of crude methanol-chloroform extracts of ants and of pure venom collected from the tip of the stinger, it was found that both preparations exhibit strong hemolytic activity. That this activity is confined to the venom was indicated by the following experiment: An extract prepared from 95 ants whose venom sacs had been carefully dissected out was found to be virtually devoid of activity, while the contents of a single sac was highly hemolytic.

The hemolytic principle appeared to be nonprotein in nature because crude extracts showed no sensible loss of activity on exposure to heat (100°C, 1 hr), the active component of extracts was soluble in a nonpolar solvent such as petroleum ether, and pure venom was Ninhydrin-negative. More insight into the nature of the hemolytic principle was gained from the observation that pure venom is alkaline in reaction and gives a positive nitrogen test, and that preparations lose their activity upon exposure to cation exchangers. These findings indicated that the hemolytic principle was associated with the alkaline constituents of the venom and was probably an amine.

These observations suggested a sensitive method of assay for at least one component of venom, the hemolytic principle, and led us to concentrate our efforts on isolating this component from crude extracts. This appeared to be preferable to our earlier plan of fractionating pure venom, the collection of which required enormous time and labor.

The method used to measure hemolytic activity is a modification of the procedure described by Wilbur and Collier (*5*). An aliquot of the material to be tested is taken up in 0.2 ml of ethanol and mixed with 3 ml of a stock suspension of washed rabbit erythrocytes in isotonic buffered saline (4.53 g of NaCl per liter of 0.067*M* phosphate buffer, *p*H 7.0). Hemolysis results in a decrease of the opacity of the suspension; this in turn is reflected in a decrease in optical density when readings are made at λ 660 mμ in a spectrophotometer. The more potent the preparation, the less time it requires to bring about hemolysis.

To isolate the hemolytic component, ants are homogenized in tissue grinders, 20 ml of methanol being used per gram of ants, and the clear extract is separated. The residue is reextracted in a similar manner with chloroform. The combined extracts are evaporated to a thick, oily mass in a flash evaporator, at 40°C. The concentrate is taken up in petroleum ether, from which medium the active material is adsorbed on silicic acid (Mallinckrodt, A. R., 100 mesh). This is then eluted with a 2:3 mixture of acetone and petroleum ether, until the effluent is free of activity. The concentrate from the eluate is taken up in a neutral, 1:1 mixture of methanol and acetone. Treatment of this preparation with carboxymethylcellulose (Brown Co., CM-S, type 20) transfers the active material to the ion exchanger. The cellulose is then treated with an excess of phosphate buffer (*p*H 7.0), 0.25*M*, and the mixture is extracted with petroleum ether followed by chloroform. The concentrate from the combined extracts is dried over phosphoric anhydride under vacuum. It is then dissolved in dry ethyl ether (about 10 ml per gram of concentrate), and the solution is chilled in an ice bath. When dry HCl is bubbled through this solution, the active principle separates as a white precipitate, presumably as the hydrochloride. This is washed free of the yellow mother liquor with more ethyl ether. It is then recrystallized twice from a mixture of carbon tetrachloride and petroleum ether and once from a mixture of ethanol and ethyl ether. Starting with a 27-g batch of ants, we obtained 160 mg of crystals and some 75 mg of less pure material.

The hydrochloride melts at 144° to 145°C, and it responds to the tests for tertiary amines. It is soluble in chloroform, carbon tetrachloride, and ethanol, slightly soluble in ethyl ether, and insoluble in water and petroleum ether. The free amine appears to be soluble in the usual fat solvents and insoluble in water.

The crystalline material is potently hemolytic: addition of 100 μg to 3 ml of the stock erythrocyte suspension brought about complete hemolysis in less than 15 seconds. The hemolytic effect is slowed considerably in the presence of serum and in systems containing cholesterol.

Further studies now in progress may enable us to assess the relationship of this substance to other constituents of the venom.

GEORGE A. ADROUNY
Department of Biochemistry, Tulane University, New Orleans, Louisiana
VINCENT J. DERBES
Department of Medicine, Tulane University School of Medicine
RODNEY C. JUNG
Department of Tropical Medicine and Public Health, Tulane University School of Medicine

References and Notes

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2. M. S. Blum, J. R. Walker, P. S. Callahan, A. F. Novak, *Science* 128, 306 (1958). This report appeared when we were in the process of studying the properties of pure venom collected by a method similar to the method described by these authors. Our findings about the venom were in agreement with theirs.
3. E. O. Wilson, *ibid.* 129, 643 (1959).
4. This work was supported by a research grant (E 1755 C-1) from the U.S. Public Health Service.
5. K. W. Wilbur and H. B. Collier, *J. Cellular Comp. Physiol.* 22, 233 (1943).

27 March 1959

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should *not* repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper.

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* 125, 16 (1957)].

A Mammalian Thioglycosidase

Abstract. A thioglycosidase capable of catalyzing the hydrolysis of 6-purine β-D-glucothiopyranoside and other thioglycosides has been found in a number of mammalian tissues (including tumors) as well as in almond emulsin. The substrate specificity of mammalian thioglycosidase involves both the aglycone and the glycosyl moieties.

In the course of a study of the relationship between chemical structure and antitumor activity among derivatives of 6-mercaptopurine, 6-purine β-D-glucothiopyranoside (MPG) and a number of related thioglycosides were synthesized (*1*). When the thioglycoside was treated with a commercial almond emulsin preparation, enzymatic hydrolysis to 6-mercaptopurine (6-MP) and glucose was observed (*1*). The marked activity of almond emulsin was surprising in view of Pigman's (*2*) report that synthetic thioglycosides do not serve as substrates for this enzyme.

In the course of antitumor trials in mice, MPG when administered intraperitoneally was found to have activity against sarcoma 180 and adenocarcinoma 755, with relatively low toxicity in comparison to its aglycone (*3, 4*). However, when MPG was administered orally, greater antitumor activity as well as increased toxicity were observed. These facts led to a study of the possible occurrence of a thioglycosidase in the digestive tract of the mouse.

Investigation showed the presence of such an enzyme, widely distributed in mammalian species and tissues, with significant activity in various rodent tumors (*5*). This was particularly surprising since enzyme preparations from animal sources, although they have been shown to contain β-glucosidase and β-glucuronidase activity (*6*), attack neither the natural thioglycosides of black mustard (*7*) nor synthetic thioglycosides (*2, 8*). No report of thioglycosidase activity from animal sources has appeared heretofore, whereas plant enzymes capable of splitting the natural thioglycosides of plants have been known for many years. Thus, the mustard thioglycosides sinigrin, sinalbin, and glucocheirolin are readily cleaved by the enzyme myrosin (*9*).

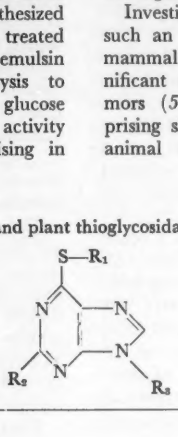
It has now been found that MPG is attacked not only by almond emulsin (*1*) but also by the thioglycosidase of the black mustard, *Brassica nigra* Koch, and by thioglycosidase preparations from a variety of animal species.

Determination of thioglycosidase activity in the studies reported here (*10*) was based on the marked differences between the ultraviolet absorption characteristics of the purinyl thioglycoside substrates and their aglycone cleavage products—6-mercaptopurine (*11*), thioguanine, and others. Tissues are readily assayed for thioglycosidase as follows: A 1:5 dilution of a tissue homogenate is prepared in saline at 0°C. One milliliter of the homogenate is incubated at 37°C for 3 hours with 5 mg of MPG at *p*H 5.8 (the optimum *p*H for thioglycosidase) in acetate buffer in a total volume of 5 ml. The solution is freed of protein by trichloroacetic acid precipitation, and the amount of 6-MP liberated by enzyme action is determined spectrophotometrically.

By means of this procedure, the presence of a thioglycoside-splitting enzyme has been demonstrated in every living species thus far examined, including man, dog, rat, mouse, pigeon, hog, and calf, and in the microorganisms *Tetrahymena pyriformis* and *Escherichia coli* (*12*).

Thioglycosidase activity was demonstrated in a number of transplantable animal tumors as follows (the numbers in parentheses describe enzyme activity in terms of micrograms of 6-MP liberated per gram of fresh tissue): sarcoma 180, solid (840); sarcoma 180, ascites (0); sarcoma T241 (717); sarcoma MA 387 (324); Ehrlich carcinoma, solid (585); Ehrlich carcinoma, ascites (0); Bashford carcinoma 63 (513); mammary adenocarcinoma E0771 (486); Miyono adenocarcinoma (500); bladder carcinoma, C57 black mouse (765); lung carcinoma, C57 black mouse (579); adenocarcinoma 755 (678); Wagner osteogenic sarcoma (500); Mecca lymphosarcoma (1188); Gardner lymphosarcoma (540); Harding-Passey mouse melanoma (500); Flexner-Jobling rat carcinoma (339); Walker carcinosarcoma 256 (1476); Jensen rat sarcoma (432); and Murphy-Sturm rat lymphosarcoma (48).

Table 1. Activities of animal and plant thioglycosidases on purinyl thioglycosides.



R_1	R_2	R_3	Activity: Mammalian thioglycosidase	Activity: Almond emulsin	Activity: Myrosin
β-D-Arabinopyranose	H	H	–		
α-L-Arabinopyranose	H	H	+		+
β-D-Galactopyranose	H	H	+	+	+
β-D-Glucopyranose*	H	H	+	+	+
β-D-Glucopyranose	NH_2	H	–		–
β-D-Glucopyranose (sulfone)	H	H	–		
β-D-Glucopyranose	NHG†	H	–		–
β-D-Glucopyranose	H	β-D-Ribofuranose	+		
β-D-Glucopyranose	H	Tri-*O*-acetyl-α-D-ribofuranose	+		
β-D-Glucofuranuronic acid*	H	H	–	–	
β-D-Glucopyranuronic acid*	H	H	–	–	
Lactose	H	H	–		–
β-D-Mannopyranose	H	H	+		+
α-L-Rhamnopyranose	H	H	–		–
β-D-Ribopyranose	H	H	–		?
2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranose	H	H	–		–
2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranose (sulfone)	H	H	–		
β-D-Xylopyranose	H	H	+		+
Miscellaneous thioglycosides					
3-Chloro-6-β-D-glucothiopyranosyl-pyridazine			–		+
2-β-D-Glucothiopyranosyl-4-pyrimidine			+		+
2,4-Dinitrophenyl β-D-glucothiopyranoside			–		+

* These compounds were tested also as substrates for bacterial β-glucuronidase and were found to be inactive. † G = a second β′-D-glucopyranosyl group.

A few samples of human malignancies have also been examined, and here too significant thioglycosidase activity was found.

Some representative values for thioglycosidase activities of normal mouse tissues are: small intestine, 5370; spleen, 2895; liver, 2100; stomach, 1626.

Mammalian thioglycosidase activity is inhibited by delta-gluconolactone at relatively high concentrations. Twenty-five-percent inhibition is produced at $10^{-3}M$, and 50 percent, at $10^{-2}M$. A number of related compounds were studied as inhibitors, including D-glucurono-δ-lactone, D-gluconic acid, D-galacturonic acid, D-galacturono-δ-lactone, D-gulono-δ-lactone, D-arabono-δ-lactone, calcium-D-arabonate, isoascorbic acid, iso-inositol, D-ribono-δ-lactone, and D-glucoheptono-δ-lactone. Of these, all were inactive with the exception of D-galactono-δ-lactone. Various other substances have been examined for activity on mammalian thioglycosidase [enzyme inhibition or no activity are indicated by (+) or (−), respectively]: $HgCl_2$ (+); NaN_3 (−); $CuSO_4$ (+); NaF (+) Na_2SO_3 (+); H_2O_2 (+); 2,4-dinitrophenol (+); 2,4-dinitrothiophenol (+); Na_3AsO_4 (+); glutathione (−); H_2S (−); cysteine (±); EDTA (−).

Further studies of the properties of the enzyme and its substrate specificity were undertaken with acetone powders of mouse intestine, hog liver, and hog pancreas (which are quite similar in thioglycosidase activity). These may be stored for at least 15 weeks at −10°C, after which time the activity slowly declines. The optimum *p*H curve is rather broad, with the maximum activity at about *p*H 5.8. The enzyme is sensitive to elevated temperatures, and heating for 5 minutes at 60°C results in a loss of 50 percent in activity; heating for 5 minutes at 70°C causes almost total inactivation. The rate of hydrolysis decreases with time; after about 3 hours under the conditions given above, the reaction finally ceases entirely, although excess enzyme and substrate are present, as shown by the fact that addition of either more substrate or more enzyme to the reaction mixture causes further hydrolysis. However, the enzymatic hydrolysis is not inhibited by the hydrolysis products.

A number of purine, pyrimidine, and other thioglycosides (*13*) have been examined as substrates for the mammalian thioglycosidase. The results are summarized in Table 1. From these results, certain generalizations may be made. The active substrates include derivatives of D-glucose, D-galactose, L-arabinose, and D-xylose, while the D-arabinoside is virtually inactive. The essential configuration required for activity is that of β-D-glucopyranose or β-D-galactopyranose. The hydroxymethyl group of C-5 may be replaced by —H, but replacement by —COOH (as in the thioglucuronides) results in loss of activity. The 6-purinyl structure is the most active aglycone found to date, but a rather wide range of aglycone variation is permitted, including purines, pyrimidines, and pyridazines.

Thus, the enzyme appears to resemble the thioglycosidase enzymes previously found only in plants and is similar to the classical β-glucosidase found in plants and animals in the structural requirements for the glycosyl residue. Furthermore, both classes of enzymes are inhibited by delta-gluconolactone (*14*).

When the presence of purinethioglycosidase at high levels of activity in tumors was first discovered, it was hoped that MPG might serve as a relatively nontoxic carrier of 6-MP, which thus would be released *in situ* in the tumor, and that the differential effect of 6-MP on tumors might thus be increased. The pharmacological properties of MPG, its rapid clearance, and its poor cellular penetration (*4*) appear to interfere with the realization of this aim. Thus, to explain the significant antitumor effects of MPG and related compounds on the basis of tumor thioglycosidase levels would appear to be premature at this point, for when MPG was administered intraperitoneally to the mouse, no evidence of cleavage to 6-MP was observed in any tissue, in spite of the demonstrated presence of thioglycosidase activity in nearly all mammalian tissues. However, orally administered MPG is rapidly hydrolyzed, liberating 6-MP in the gut.

No clues to the occurrence of natural substrates for this thioglycosidase have yet been found. Its high level of activity and wide distribution are all the more puzzling since MPG appears to possess the optimal substrate configuration.

IRVING GOODMAN*, JAMES R. FOUTS†, EDWARD BRESNICK, ROSALIE MENEGAS, GEORGE H. HITCHINGS

Wellcome Research Laboratories, Tuckahoe, New York

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11. Absorption maxima and molecular extinctions at *p*H 6: for 6-MP; $\lambda_{max.} = 320$ mμ, $E_m = 18.9 \times 10^3$; for MPG, $\lambda_{max.} = 280$ mμ, $E_m = 16.0 \times 10^3$.
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* Present address: Department of Biochemistry, Columbia University, New York, N.Y.
† Present address: State University of Iowa, Iowa City.

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Learning Differences in Two Separated Lines of Mice

Abstract. Significant differences in conditioning and response topography were obtained with two lines in C57BL/10 mice, suggesting the occurrence of a behavioral mutation. It is suggested that the two lines be classified as substrains. The two substrains would appear to be useful in experiments on the genetics of behavior.

In the summer of 1957 while working at the Behavior Laboratory of the Roscoe B. Jackson Memorial Laboratory (*1*), I found that 150-day-old C57BL/10 mice had a significantly higher conditioning score than did equivalent mice tested the previous year in a different study (*2*). In trying to determine the cause of this difference, I noted that the mice used in 1957 had come from the colony at the Main Laboratory while the mice tested in 1956 had come from the Behavior Laboratory. Mice from the Behavior Laboratory colony which were 150 days old were then tested and found to have a mean conditioning score very similar to the mean obtained the previous year with the Behavior Laboratory animals. A number of 50-day-old mice were available from both laboratories and were also tested. The same phenomenon was obtained: the mean score of the Behavior Laboratory mice in 1957 was not significantly different from that of the Behavior Laboratory mice tested in 1956, while the Main Laboratory animals were again significantly better on the conditioning task.

These findings suggested either that there had been some genetic change or that the environmental rearing conditions in the two laboratories were different enough to affect conditioning ability differentially. To determine whether these differences were simply correlated

Table 1. Summary statistics on conditioning of 50-day-old mice by year of testing, laboratory strain, and filial generation.

Year	$\bar{X}$	s	n	Generation
		Behavior Laboratory		
1956	1.80	2.30	10	*
1957	2.17	2.23	6	F_{64}, F_{65}
1958	1.45	1.13	11	F_{67}
Total	1.74	1.83	27	
		Main Laboratory		
1957	4.21	1.93	14	F_{57}, F_{58}
1958	4.44	1.51	9	F_{60}, F_{61}
Total	4.30	1.76	23	

* Unknown.

with place of rearing, pregnant mice from the Main Laboratory colony were brought to the Behavior Laboratory in the summer of 1958, and their offspring were reared and tested under the same environmental conditions as the Behavior Laboratory animals. Both groups were tested at 50 days of age.

The conditioning procedure, described fully elsewhere (*2*), consisted essentially of presenting a 3-second buzzer which was always followed immediately by 1 second of shock. Forty-one seconds later the buzzer-shock sequence was repeated. Ten such trials were given. The conditioned response was defined as any gross movement by the mouse during the interval that the buzzer was on. For each trial the animal received either a score of 0 for no response or a score of 1 for a conditioned response. Since the mouse could not make a conditioned response on the first trial, the maximum possible score was 9. Table 1 summarizes the pertinent statistics by year, laboratory strain, and filial generation. The mice from the Behavior Laboratory were all reared and tested there. The Main Laboratory mice in 1957 were reared there and then sent over to the Behavior Laboratory, where they were tested; in 1958 they were reared and tested at the Behavior Laboratory. Within each laboratory strain the means do not differ significantly, while the mean difference between laboratory strains is significant beyond the .01 level.

A further analysis of the 1958 data showed that the type of conditioned response differed between the strains. Of the 16 responses made by the Behavior Laboratory mice, 13 were runs and three were jumps. This finding is consistent with the results obtained in 1956 (*2*). However, of the 40 responses elicited by the Main Laboratory mice, 30 were jumps and ten were runs.

The Behavior Laboratory and the Main Laboratory mice were separated in 1947 at F_{32}, and each strain has passed through approximately 30 generations since then, during which time a mutation is likely to have occurred which could have caused the obtained behavioral differences. Since the strains have been apart for more than the 15 to 20 generations of separated breeding which has been specified in the definition of a substrain (*3*), it is evident that these two groups should be considered substrains. It is suggested that the Main Laboratory mice be designated C57BL/10Jax, while the Behavior Laboratory mice maintained by J. P. Scott would continue to be called C57BL/10Sc.

The results suggest that a behavioral mutation has occurred which affects learning capacity and response topography. Thus, these two substrains would appear to be useful for experiments on the genetics of behavior. Another implication of these data is the important methodological consideration that, even when highly inbred animals are used, care should be taken to use as experimental subjects only animals which are closely related in terms of filial generation (*4*).

VICTOR H. DENENBERG
Department of Psychology, Purdue University, Lafayette, Indiana
and *Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine*

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10-Hydroxy-Δ^2-Decenoic Acid, an Antibiotic Found in Royal Jelly

Abstract. 10-Hydroxy-Δ^2-decenoic acid, the major component of the lipide fraction of royal jelly, exhibits antibiotic activity against many bacteria and fungi. This fatty acid is less than one-fourth as active as penicillin against *Micrococcus pyogenes* and less than one-fifth as active as chlortetracycline against *Escherichia coli*. It also slows the growth rate of *Neurospora sitophila* and some unidentified molds. The salt of this compound is considerably less active than the free acid.

The presence of antimicrobial activity in the royal jelly of the honey bee (*Apis mellifera* L.) has been known for 20 years. McCleskey and Melampy (*1*) demonstrated that, although royal jelly inhibited the growth of both Gram-positive and Gram-negative bacteria, it was about twice as effective against the Gram-positive organisms. More recent investigations (*2*) have shown that both royal jelly and its extracts exhibit antibiotic activity against a variety of microorganisms. Other investigators (*3*) have been unable to demonstrate antibacterial activity in royal jelly. This discrepancy may be explained by the fact that the various investigators have tested royal jelly samples of different ages and that the antibacterial activity of royal jelly diminishes with age (*4*).

McCleskey and Melampy (*1*) showed that the antibacterial component of royal jelly was soluble in either acetone or alcohol and was present in concentrates of the fatty acid and nonsaponifiable fraction. Abbott and French (*5*) suggested that a fatty acid was at least partially responsible for the ability of royal jelly to resist bacterial and fungal infestations. They further suggested that the high sugar content of royal jelly may also contribute to its ability to inhibit the growth of microorganisms. Fractionation of royal jelly in this laboratory has shown that its antibiotic properties result solely from the presence of an unusual fatty acid, 10-hydroxy-Δ^2-decenoic acid, isolated from royal jelly by Butenandt and Rembold (*6*) and more recently by Barker *et al.* (*7*), who reported little activity against bacteria and fungi.

Royal jelly was collected from queen cells and immediately frozen (−16°C). The frozen royal jelly (90 g) was lyophilized, yielding a cream-colored powder (30 g) which inhibited the growth of *Escherichia coli* and *Micrococcus pyogenes* when tested by the paper disc method. The powder was then extracted for 72 hours with ethyl ether in order to remove the lipide components (2.9 g). The remaining powder was inactive against the test organisms, but the ether extract was active. The ethereal solution was extracted with 2*N* KOH. This alkaline extract was acidified with 0.1*N* H_2SO_4, and the free acids were extracted from it with ethyl ether. Removal of the ether on a steam bath yielded a thick yellow gum (2.59 g). The neutral lipide fraction was inactive, proving that the antibiotic principle found in royal jelly is in the fatty acid fraction.

The fatty acid fraction was dissolved in warm 50-percent ethyl alcohol and kept at −10°C for 24 hours. The acid precipitated as thin white crystals which were collected and recrystallized from 50-percent ethyl alcohol. The acid melted at 56° to 57°C. Carbon-hydrogen analyses indicated an empirical formula of $C_{10}H_{18}O_3$. The infrared spectrum of the acid showed the presence of a hydroxyl band at 2.97 μ and an unsaturation band at 6.05 μ, which is characteristic of a hydroxy-unsaturated acid. All data are in agreement for 10-hydroxy-Δ^2-decenoic acid. By means of a mixed melting point and an infrared comparison with a pure sample of this acid (*8*), its structure was confirmed.

The pure acid was tested on strains of *Escherichia coli* and *Micrococcus pyogenes* by incubating both organisms in antibiotic assay media fortified with serial dilutions of the acid. Comparison with penicillin (*M. pyogenes*) and chlortetracycline (*E. coli*) indicated that this fatty acid was less than one-fourth as active as penicillin and less than one-fifth as active as chlortetracycline. In this procedure, the activity cannot be attributed solely to any change in *p*H produced by incorporating the acid into the medium, because each serial dilution was adjusted to *p*H 6.7 after the substance was added.

When 10-hydroxy-Δ^2-decenoic acid was evaluated by the paper disc method, neither of these organisms was able to grow in the presence of an impregnated disc during a 14-day period. However, when the salt was tested by the same procedure, the activity was considerably less than that of the free acid. Conversion of the acid to the salt may explain why royal jelly loses its bactericidal activity when neutralized or made slightly alkaline (*9*).

10-Hydroxy-Δ^2-decenoic acid also inhibited the growth of *Neurospora sitophila* as well as several unidentified molds. The antibiotic activity of this acid merits attention because it is active against both bacteria and fungi.

Townsend *et al.* (*10*) reported that admixture of royal jelly with tumor cells before inoculation completely suppresses the development of a transplantable mouse leukemia and the formation of ascitic tumors in mice. Fractionation showed this antitumor activity arises from the main fatty acid of royal jelly: 10-hydroxy-Δ^2-decenoic acid.

This growth inhibiting fatty acid is related to another natural product, the wound hormone of plants, traumatic acid (Δ^1-decene-1, 10-dicarboxylic acid) (*11*). Growth-inhibiting properties have also been demonstrated for other fatty acids (*12*), particularly for undecylenic acid against bacteria (*13*) and fungi (*14*).

It is not surprising that royal jelly contains a substance inhibiting the growth of microorganisms, since it would otherwise be an excellent substrate for bacterial growth. The origin of this fatty acid in royal jelly is now being investigated.

MURRAY S. BLUM
Entomology Research Department, Louisiana State University, Baton Rouge

ARTHUR F. NOVAK
Department of Agricultural Chemistry and Biochemistry, Louisiana State University

STEPHEN TABER, III
Agricultural Research Service, U.S. Department of Agriculture, Washington, D.C.

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Inhibition of O-Methyltransferase by Catechol and Sensitization to Epinephrine

Abstract. Catechol at equimolecular concentration inhibits the inactivation of adrenaline by O-methyltransferase in vitro about 50 percent. The inhibition is probably responsible for the sensitization of smooth muscles to epinephrine by various ortho di- or triphenols.

One of us (Z.M.B.) described in 1936 a remarkable potentiation of the effects of epinephrine on various smooth muscles of the cat (nictitating membrane, spleen, uterus, blood vessels) after injection of catechol or pyrogallol, but not of resorcinol (*1*).

The interpretation, at that time, was that the sensitizing phenols slowed down the oxidation of epinephrine by virtue of their well-known antioxidant action.

A new interpretation becomes highly probable after the demonstration by Axelrod *et al.* that epinephrine is inactivated by an O-methyltransferase which methylates the phenolic OH in position 3 (*2*). It seems that epinephrine is not a specific substrate, that other ortho-diphenols are also methylated by this enzyme. Thus, logically, catechol might sensitize in vivo by competitive inhibition of the methyltransferase.

The following simple test strongly suggests that such an inhibition occurs in vitro. In the reaction studied by Axelrod, the methyl donor is S-adenosylmethionine—that is, methionine activated by adenosine triphosphate (ATP). We have prepared a solution of enzymes containing the methyltransferase and the methionine-activating enzyme by precipitating a particle-free supernatant of rat liver homogenate (1 hour at 105,000 *g*) with ammonium sulfate (90 percent saturation) and dissolving the precipitate in $KHCO_3$. This solution, in the presence of a sufficiently high concentration of methionine and ATP, inactivates epinephrine.

The conditions are as follows: 0.6 to 0.4 μmole of adrenaline is incubated at 37°C for 45 minutes with 1 ml of the enzyme solution, in the presence of $MgCl_2$ (10 μmole/ml) in phosphate buffer (*p*H 7.6) (100 μmole/ml). The final volume is 2 ml. The quantities of ATP and methionine necessary to inactivate 70 percent of the epinephrine are about 10 μmole each; greater quantities do not increase the percentage of inactivation and interfere with biological titration. After incubation, proteins are precipitated by trichloracetic acid (5 percent) and centrifuged. Epinephrine is titrated by fluorescence (*3*) and by its action on the blood pressure and nictitating membrane in the cocainized cat.

During incubation, part of the epinephrine is inactivated, probably by auto-oxidation. If one adds an equimolecular amount of catechol to the system, the percentage of enzymatic inac-

Table 1. Influence of catechol on the inactivation of epinephrine by incubation with soluble enzymes of rat liver in the presence of ATP and methionine.

Experimental conditions				After incubation		
Tube No.	Epinephrine (μmole)	Catechol (μmole)	ATP and *l*-methionine (μmole)	Fluorescence (%)	Epinephrine (μmole/ml)	Inactivation (%)
1	0.4			61.5	0.08	0
2	0.4		10	18.5	0.024	71
3		0.4		2		
4		0.4	10	4		
5	0.4	0.4		62.5	0.081	0
6	0.4	0.4	10	36	0.047	42
7		0.8		2		
8	0.4	0.8		58	0.075	7.5
9	0.4	0.8	10	53	0.069	15

tivation falls from 71 to 42 percent; with double the concentration of catechol, only 15 percent of the epinephrine is inactivated (Table 1). Neither ATP nor catechol interferes with chemical titration; ATP interferes with biological titration only at high doses. Biological tests have confirmed the results obtained with the fluorescence method.

Many plant phenolics with a catechol nucleus sensitize smooth muscle to epinephrine (*4*); inhibition of methyltransferase is probably the responsible mechanism.

The facts (i) that, in vivo, iproniazid or any inhibitor of amino oxidase does not sensitize to epinephrine or adrenergic nerve stimulation and (ii) that inhibitors of O-methyltransferase do sensitize in vivo are powerful arguments in favor of the opinion that methyltransferase (and not amino oxidase) is the enzyme which normally inactivates the bulk of catecholamines in mammals (see *5*).

ZENON M. BACQ, LUC GOSSELIN, ALBERT DRESSE, JEAN RENSON
Department of General Pathology and
Institute of Physiology,
University of Liège, Belgium

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5 June 1959

Prolactin, a Factor in Promoting Survival of Hypophysectomized Killifish in Fresh Water

Abstract. The naturally occurring corticosteroids, cortisol and aldosterone, failed to promote survival of hypophysectomized *Fundulus heteroclitus* in fresh water. Extracts of *Fundulus* interrenal tissue, carp corpuscles of Stannius, and hog renin were ineffective. Injection of whole rat-pituitary brei was partially successful. Highly purified prolactin maintained survival, although the recipients did not eat normally. A synergic action of prolactin with some unidentified pituitary hormone is suspected.

Burden (*1*) showed that the hypophysectomized and normally euryhaline killifish, *Fundulus heteroclitus,* is unable to survive in fresh water. Death results from progressive asthenia, correlated with hypochloremia, which becomes severe after 6 to 7 days at 15° to 17°C. Replacement therapy with *Fundulus* pituitary brei was completely successful; perch pituitary was partially effective, but pollack pituitary gave negative results. Mammalian pituitary hormones (TSH, ACTH GH, and posterior lobe powder) were ineffective. Lack of participation of the thyroid was confirmed by administration of thyroxin. More recently, Harris (*2*) found that hypothyroidism, resulting from treatment with I^{131}, had no detrimental effect on the survival or blood chloride levels of this species in fresh water. Burden suggested that a special agent, regulating adaptation to fresh water, was present in the pituitary of teleosts living in this medium.

In Burden's experiments lack of participation of the adrenal, indicated by failure of natural stimulation with exogenous ACTH, was partially confirmed by negative results with DOCA. Recent studies by one of us (*3*) showed that the circulating glucocorticoid of *Fundulus* is cortisol. Moreover, incubation of the head kidney, containing the adrenocortical (interrenal) tissue, with tritiated progesterone results in the synthesis not only of cortisol but also of other steroids, including aldosterone (*4*). An investigation was therefore undertaken to study the possible participation of these natural steroids in the survival of killifish in fresh water.

Hypophysectomized fish, pretested for failure to withstand fresh water, were rescued at the onset of severe symptoms and allowed to recover in salt water. Each experimental group contained four such fish. Hormones or extracts dissolved in 0.6-percent NaCl were administered by intraperitoneal injection on alternate days, at constant volume (0.01 ml/g wt. of fish). The temperature was 15° to 16°C except at the higher dose of cortisol, which was tested at 20°C. It was noted that failure in fresh water is accelerated at the higher temperature. Negative results were obtained with cortisol (2.5 and 0.0025 μg/g wt.), aldosterone (24 and 2.4 μμg/wt.) and extracts of right and left head kidney of *Fundulus* [20 mg (wet wt.)/g wt.] The lower doses of cortisol and aldosterone were considered to be at physiological levels. The right head kidney contains the major part of the adrenal tissue in this species (*5*).

These results, and those of Burden, indicate that the adrenal plays no direct role in regulating survival of *Fundulus* in fresh water. This is in accordance with recent work of Holmes (*6*), who found that in rainbow trout cortical steroids promoted renal salt retention, under a salt load, but that this effect was offset by an enhanced loss of salt through the gills and inhibited re-uptake. Different results have been reported, however, for the goldfish (*7*).

Other hormones that might be concerned with teleostean osmoregulation were considered. The gonadotropins and sex steroids can presumably be excluded, since fish of either sex, juvenile, mature, or in seasonal regression, can move freely from salt to fresh water. On the other hand, the corpuscles of Stannius may play some role in osmoregulation (*8*), although there is no evidence that these glands are regulated by the pituitary (*5*); however, a brei of carp corpuscles of Stannius [1 mg (wet wt.)/g wt.] gave negative results. Renin, said to be present in the kidneys of fresh-water but not in those of marine teleosts (*9*), was tested at two dosages (50 μg/g wt. on alternate days; 5 μg/g wt. daily) without beneficial action.

The possible participation of an unidentified mammalian hypophysial hormone was tested with whole rat-pituitary brei [1 mg (wet wt.)/g wt.]: two fish out of four survived for 20 days but refused to eat, and neither recovered in salt water.

Prolactin, which is known to be present in the teleostean hypophysis (*10*) and which initiates the "water drive" in efts of *Triturus* (*11*), was tested (10 μg/g wt.) with unexpectedly successful results. All four recipients survived for 20 days and remained lively, although they ate little. A combination of prolactin with some other pituitary hormone may be necessary for complete adaptation to fresh water, and investigations of this aspect of the problem are in progress. The synergic action of prolactin is well known in mammalian endocrinology, and its function in potentiating the melanophore-proliferating effect of intermedin in *Fundulus* has been established (*12*). The ineffectiveness of pollack pituitary brei, reported by Burden, may be correlated with the low prolactin content of this material (*10*). Rat pituitary, on the other hand, evidently, contains sufficient prolactin to be partially effective (*13*).

GRACE E. PICKFORD
JOHN G. PHILLIPS*
Bingham Oceanographic Laboratory,
Yale University,
New Haven, Connecticut

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13. This investigation was supported by a grant from the National Science Foundation (NSF G-4001). We should like to thank the following for donating hormones used in this study: A. A. Renzi (aldosterone); Choh Hao Li (highly purified prolactin); and Irvine H. Page [hog renin (assay: 10 mg caused a rise of 100 mm of Hg in the dog)].
* Fellow of the Commonwealth Fund of New York. Present address: Department of Zoology, Sheffield University, England.

20 March 1959

Differentiation of Activity of Three Mouse Strains with Magnetic Pickup Apparatus

Abstract. An activity pickup, when used with a high-gain amplifier, permits records to be made of essentially all the activity of a mouse. The sensitivity is such that the differences in the activity patterns of strains of mice can be determined.

When the activity of small animals is appraised, the animal is usually required to cause movement of a relatively large mass, most commonly a pan or an entire cage, which is then connected to a recording device of some sort (*1*). Problems frequently encountered in such apparatus are incomplete recording of activity, artifacts due to resonance, and feedback to the animal due to pan or cage inertia and noise in the recording apparatus.

The apparatus described in this report (*2*) apparently circumvents all these difficulties. The activity pickup employs the principle of movements of a small iron plate which induces electric current in a coil with a bar magnet core. The currents thus produced are amplified electronically and recorded as activity.

Figure 1 shows the apparatus schematically. Movements of the mouse or other small animal cause micromovements of the galvanized iron plate *A*. Magnetic lines of force flowing between the poles of the magnet *NS* are altered by the movement of the plate, and thus current proportional to the movement is induced in the windings; the current is fed (*C*) to a preamplifier, amplifier, and recorder. Specifications are as follows: *A*, galvanized iron plate, 22 gauge, 3 by 4 in.; *B*, latex tubing, ½ in., ¼ in. I.D., cemented to the plate by rubber-to-metal cement. *NS*, 3-in. bar magnet wound with one layer of magnet wire. The specifications are for a mouse apparatus; with slight changes the apparatus could be adapted to larger or smaller animals. A Grass EEG machine was used for amplification and recording.

The plate is doubly damped, by the latex tubing and the attraction of the magnet, and resonance is kept to a minimum without friction. Use of larger plates tended to cause resonance. Three such plates were used, the leads being connected in parallel. For multiple-plate recording, adjacent magnets should be arranged with like polarity (or repulsion) for maximum sensitivity. Clear plastic walls of dimensions that allow 1/16-in. clearance of the plates act as the cage and permit observation of the mouse. All exposed wire is covered with rubber tubing to protect it from urine. The plate is built up to allow ½-in. clearance between the magnet and the plate. The apparatus is mounted on firmly damped ¼-in. mesh screening material.

Sensitivity is such that virtually all activity can be recorded, from shaking and trembling to running and jumping. Artifacts appear to be minimal or absent. On the records obtained, activity resolves into three major components: (i) large discrete deflections, correlated with jumping, jerking, and sudden movements in general; (ii) moderate, continuous deflections, correlated with walking, shaking, trembling, and scratching; (iii) quiet periods.

Figure 2 shows representative records of three mouse strains. Ten male mice were tested in each strain, and the activity patterns illustrated are characteristic for the given strains. The top record is of *Peromyscus gracilis*, a wild mouse exhibiting much running and jumping behavior. The middle line shows activity of strain C57BL/6, an aggressive, fighting mouse, which is characterized by many sudden movements with a moderate amount of continuous activity. Strain A/JAX, a standard laboratory albino, shows less activity of all kinds than the other two strains.

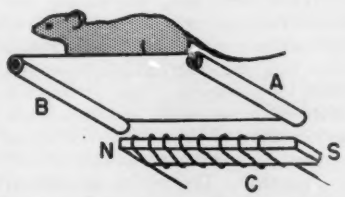

Fig. 1. Schematic representation of pickup apparatus.

Fig. 2. Records of characteristic activity patterns of three different strains of male mice: (top) *Peromyscus gracilis*; (middle) C57BL/6; (bottom) A/JAX.

The sensitivity of the activity pickup apparatus described suggests possible application in psychopharmacological studies.

WALTER G. MITCHELL*
Hamilton Station, Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine

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* Present address: Box 281, Crozet, Va.

2 April 1959

Tartaric Acid Metabolism of Neurospora crassa

Abstract. The growth of wild type *Neurospora crassa* is stimulated by various organic acids including tartaric, tartronic, and mesoxalic acids. Evidence is presented that this organism converts *d*- or *l*-tartaric acid to tartronic and mesoxalic acid, probably by fixation of CO_2.

The function of tartaric acid has been a biochemical enigma since Pasteur initiated research on this substance. Recently its metabolism by several organisms or tissues has been reported with varying results. Cleland and Johnson (*1*) find that it is converted quantitatively to oxalate by *Aspergillus niger*. Nomura and Sakaguchi (*2*) find that the principal product is succinate with *Pseudomonas incognita*, while Kun and Hernandez (*3*) propose that, with animal mitochondria, the first product is oxaloglycolic acid which can then be converted to a number of products, including diketosuccinic acid and glyoxylic acid. When, therefore, we found that *Neurospora crassa* is stimulated by tartrate as well as by several other organic acids, we made an effort to determine the mechanism of this stimulation and the fate of the tartrate.

Conidia were taken from cultures of *Neurospora crassa*, strain 74A (wild type), grown on minimal medium (*4*) with 2 percent (wt./vol.) sucrose and 1.5 percent (wt./vol.) agar. Aliquots were inoculated into 20-ml portions of Westergaard-Mitchell medium (*5*) containing 2 percent (wt./vol.) sucrose and supplements. Pads were harvested after 72 hours, dried, and weighed.

Among the organic acids which were

found stimulatory were tartaric, mesoxalic, and tartronic acids, and all the acids of the citric acid cycle that were tested. It was thought possible that tartrate might be decarboxylated to tartronate and the latter oxidized to mesoxalate, as has been observed in other organisms (*6*). Fresh mycelial pads, grown in 10 m*M* tartrate, were shaken in 0.1 *M* phosphate buffer of *p*H 5.0, alone or with 10 m*M* tartrate, tartronate, or mesoxalate, for up to 5 hours. The buffer was exhaustively extracted with ether, and the organic acids were chromatographed with three different solvents. When the pad was shaken with buffer alone, only citrate appeared in the extract. When it was shaken with *d*-tartrate, then citrate, tartrate, tartronate, and mesoxalate appeared. When it was exposed to tartronate; citrate, tartronate and mesoxalate appeared on the chromatograms, and when it was shaken with mesoxalate, only citrate and mesoxalate could be detected.

Table 1. Adaptation of *Neurospora crassa* strain 74A to various organic acids. Conidia were inoculated into 20 ml of Westergaard-Mitchell medium containing 2 m*M* of the "initial" acids indicated below. After 24.5 hours, 0.2 ml of a *p*H-5.5 aseptic solution of other acid was added (or in the case of "None," 0.2 ml of sterile water). Mycelium was dried and weighed after 3 days' growth. Weights reported are averages of four replicates.

Acid added after 24.5 hr	Wt. of mycelium (mg)	Standard deviation
Initial acid: d-*Tartrate*		
None	33.1	0.2
Malate	41.6	0.3
d-Tartrate	47.5*	1.2
l-Tartrate	47.5*	0.0
meso-Tartrate	41.4	0.0
Tartronate	47.7*	0.4
Mesoxalate	48.2*	0.9
Initial acid: l-*Tartrate*		
None	34.5	0.6
Malate	41.6	1.0
d-Tartrate	50.1*	0.1
l-Tartrate	47.8*	1.7
meso-Tartrate	46.5*	1.0
Tartronate	48.7*	0.4
Mesoxalate	49.8*	1.0
Initial acid: meso-*Tartrate*		
None	33.6	0.0
Malate	44.3	0.9
d-Tartrate	49.6	1.6
l-Tartrate	46.7	3.1
meso-Tartrate	46.1	1.2
Tartronate	54.3	3.6
Mesoxalate	48.2	2.1
Initial acid: Tartronate		
None	38.1	0.5
Malate	42.4	0.8
d-Tartrate	40.4	0.5
l-Tartrate	42.2	0.8
meso-Tartrate	38.1	1.6
Tartronate	48.1*	0.2
Mesoxalate	47.2*	0.8
Initial acid: Mesoxalate		
None	36.0	1.2
Malate	41.0	0.9
d-Tartrate	41.5	0.1
l-Tartrate	41.1	0.1
meso-Tartrate	42.2	0.1
Tartronate	43.3	0.8
Mesoxalate	48.5*	1.9

* Weight significantly greater than that obtained by adding malate after 24.5 hr (adapted response).

Strain 74A was grown for 1 day in the presence of 2 m*M* concentration of an organic acid. After this, further organic acid was added in 6 m*M* concentration, and the dry weight attained after 3 days was assayed. An adapted response was defined as the growth attained when the same acid was added as was initially present. If the growth attained was significantly below this value, that was considered an unadapted response. The results appear in Table 1.

The results indicate that when *Neurospora crassa* was exposed to *d*- or *l*-tartrate, it was adapted to *d*-tartrate, *l*-tartrate, tartronate, mesoxalate, and possibly to *meso*-tartrate (results obtained with *meso*-tartrate were more variable than with the other acids). When exposed to tartronate, this strain was adapted to tartronate and mesoxalate and to none of the others. *Neurospora* exposed to mesoxalate was adapted only to mesoxalate. The results obtained by exposing initially to *meso*-tartrate seem best explained on the basis that the organism was not thus adapted to any organic acid, including *meso*-tartrate itself. Malate was introduced as an acid to which the organism might be expected not to become adapted by exposure to any of the other acids used.

Fresh mycelium was shaken with tartrate and *p*H-5 buffer in a Warburg apparatus with the results shown in Fig. 1. The CO_2 output was reduced by 3.8 µmole, 2 mole/mole of tartrate, the same results being obtained with *d*- and *l*-tartrate, and with fresh mycelium and mycelium which had been soaked in acetone and dried. *meso*-Tartrate had

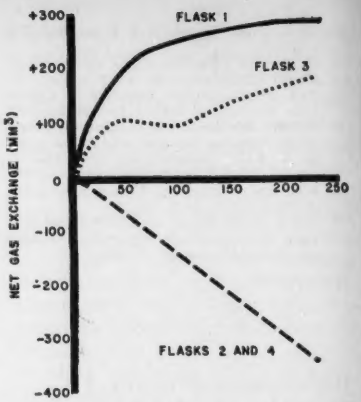

Fig. 1. Effect of *d*-tartaric acid on the respiration of *Neurospora crassa*. All flasks contained fresh mycelium and 0.1*M* phosphate buffer at *p*H 5.0. Flasks 2 and 4 contained 20 percent NaOH to absorb the CO_2 evolved. Flasks 3 and 4 contained 0.7 ml 2.8 m*M* *d*-tartrate (1.9 µmole). The results have been corrected to constant mycelial weight. The difference between the CO_2 evolved by flasks 3 and 4 is 3.8 µmole and was constant for the last 75 minutes of the experiment.

no significant effect on CO_2 output or O_2 consumption. These results suggest that tartrate is converted to mesoxalate and tartronate by the following mechanism:

$$\text{HOOC—CHOH—CHOH—COOH} + 2CO_2 \rightarrow \text{HOOC—CO—COOH} + \text{HOOC—CHOH—COOH}$$

and that tartronate is oxidized to mesoxalate:

$$\text{HOOC—CHOH—COOH} + \tfrac{1}{2}(O_2) \rightarrow \text{HOOC—CO—COOH} + H_2O$$

An investigation of the possible mechanism of stimulation of growth in *Neurospora crassa* by tartronate and mesoxalate was also made (*9*).

S. W. Bowne, Jr.*
Eastern Washington College of Education, Cheney

Adrian M. Srb
Plant Breeding Department, Cornell University, Ithaca, New York

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8. This investigation was supported by research grant C-1256 from the National Institutes of Health, U.S. Public Health Service.
9. A description of the results of this investigation is in preparation.

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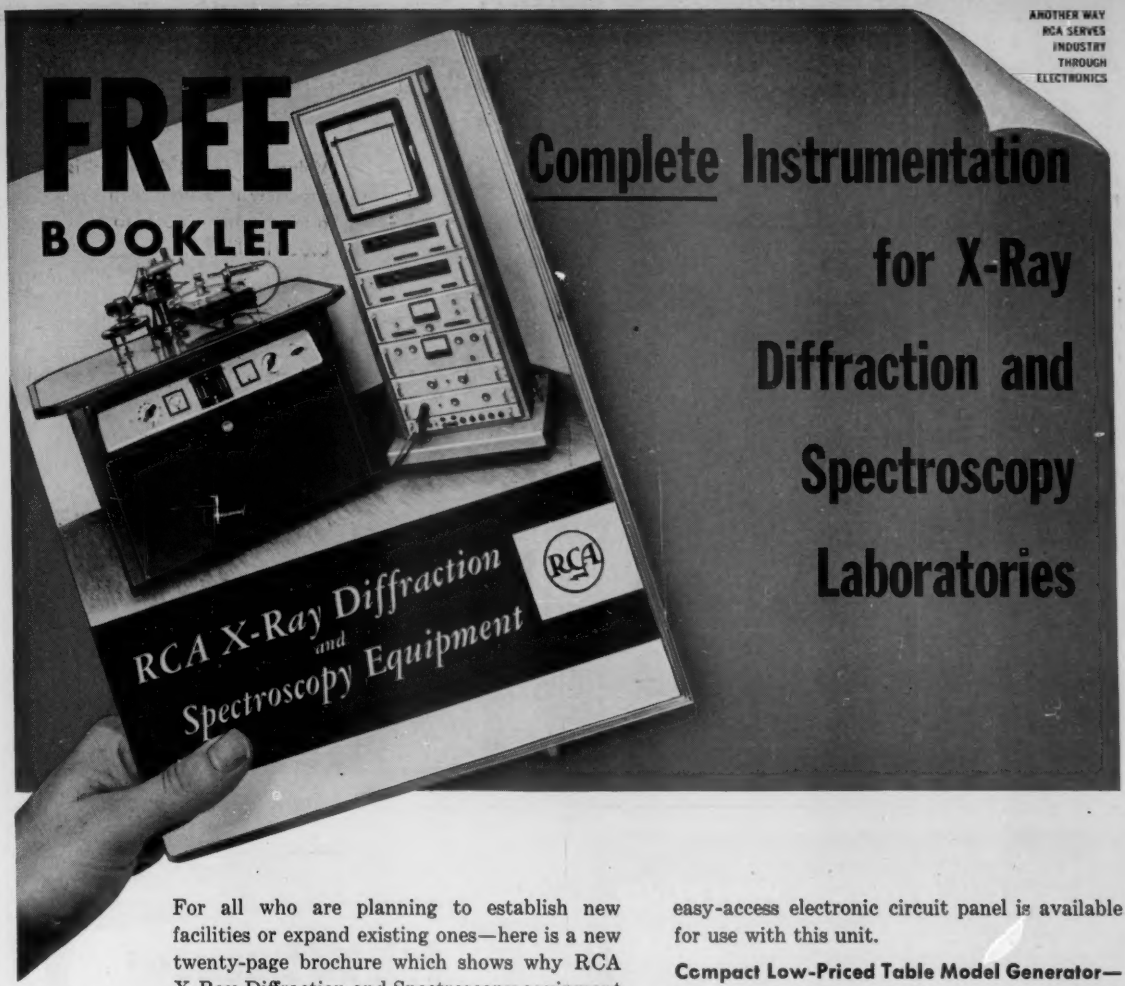

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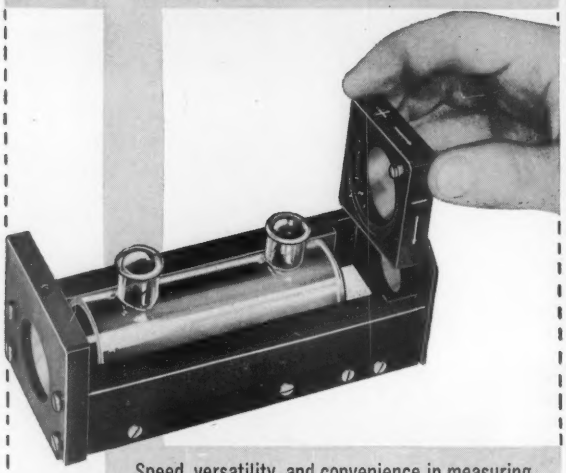

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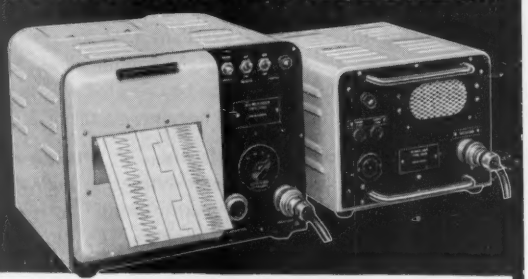

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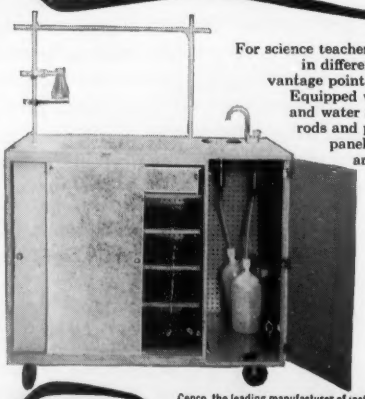

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Meetings

Allergen Standardization

More than 30 of the nation's top research immunologists participated in a one-day scientific conference on the problem of allergen standardization, held at the National Institutes of Health on 13 June. The participating scientists reached general agreement on a concrete program which, it is hoped, will eventually provide model systems for the purification of ragweed pollen and other allergens.

For three decades, allergen standardization has been singled out as the most important consideration in the field of clinical allergy. Most authorities in the field agree that the scientific investigator must be provided with allergenic products meeting rigid norms of potency, purity, and specificity before substantial progress can be made in this area of immunological research. At the present time, investigators are frequently unable to test for specific irritants, since most allergenic extracts are crude preparations composed of several components presumably related to the specific sensitization under investigation.

Aware that newer purification techniques promise progress toward a solution of the problem, the National Advisory Allergy and Infectious Disease Council of the National Institutes of Health last year appointed an *ad hoc* committee to assess present activities in this area and to consider future plans. Members included Jules Freund, National Institute of Allergy and Infectious Diseases; Dan Campbell, California Institute of Technology; Merrill Chase, the Rockefeller Institute for Medical Research; Bram Rose, McGill University, Montreal; William Sherman, Columbia University; Roderick Murray, director, Division of Biologics Standards, National Institutes of Health; Irvin Kerlan, Food and Drug Administration; and Harry Alexander, emeritus professor, Washington University, St. Louis (chairman of the committee).

At a meeting held in November 1958, the members learned that three investigators—A. R. Goldfarb, of the Chicago Medical School; Bram Rose; and Einer Hammarsten of the Karolinska Institute, Stockholm—employing dissimilar chemicophysical methods and working independently, had obtained highly purified and potent fractions of ragweed pollen, the most important single allergen in this country. These fractions, although not yet compared, were presumed to be similar in constitution. As a result, the committee recommended to the council that funds be provided to interested scientific investigators for characterizing and comparing the three products to determine whether or not they were equivalent and, if possible, to create a template for future investigations of other allergens.

The council then established a permanent committee under the chairmanship of Campbell, who was authorized to expand its base to include representatives of other government agencies and of industry when the program reached the proper stage of development.

The recent conference held under the auspices of the council provided a forum at which the scientists were able to reexamine the unsolved elements of the problem and develop a definite course of action in several specific areas. As one of the primary areas, the immunochemical identification of ragweed pollens was assigned to a task force under the direction of Chase. The several chemists who have fractionated this pollen agreed that their respective methods should be repeated by others to assure reproducibility. Previously, steps had been taken by the committee to assure availability of the pollen to the participating chemists.

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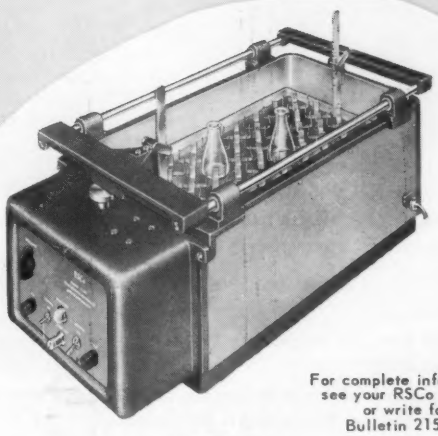

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Instrument-Automation Conference

Programs for 60 technical sessions have been arranged for the 14th annual Instrument-Automation Conference and Exhibit of the Instrument Society of America that will take place in Chicago, 21–25 September. The total number of sessions sets a new ISA conference record.

While the nearly 200 presentations will cover virtually the entire range of recent developments in instrumentation for science and technology, more conference time has been assigned to problems of computer control for industrial processes than to any other subject.

Arrangements have been made through the International Federation for Automatic Control for sessions on instrumentation developments abroad. Technical sessions will be held in the Palmer House and the Hotel Morrison, and some 350 exhibits will be shown in the Chicago International Amphitheatre.

Clinical Chemists

The American Association of Clinical Chemists will hold its 11th annual meeting at Western Reserve University, 27–29 August. Some 58 papers will be presented, and two symposia are scheduled. The first will be on the spectrophotometric method of analysis (visible, ultraviolet, and fluorometric) and the second will be a discussion of the professional status of clinical chemists. Information may be obtained from D. J. Waide Price, Institute of Pathology, Western Reserve University, 2065 Adelbert Rd., Cleveland 6, Ohio.

Nonspecific Resistance

Fort Detrick, in Frederick, Md., will sponsor a symposium on nonspecific resistance to infection on 16 and 17 September. The conference, which is being arranged in cooperation with the American Institute of Biological Sciences, will be held at Hood College, Frederick.

An international representation of specialists in this field of research will summarize their views. Visitors from abroad will include Henry Harris, Sir William Dunn School of Pathology, University of

Oxford, Oxford, England; Derrick Rowley, Wright-Fleming Institute of Microbiology, St. Marys Hospital, London, England; and David W. Henderson, Microbiological Research Establishment, Porton, Wiltshire, England. The program was organized by the conference chairman, Colin M. MacLeod of the University of Pennsylvania, together with Ivan L. Bennett, Jr., and Leighton E. Cluff, of Johns Hopkins University, René J. Dubos of the Rockefeller Institute for Medical Research, and Harold N. Glassman, assistant scientific director at Fort Detrick.

The proceedings will be published, with individual chapters somewhat expanded beyond the verbal presentations. Cluff will prepare a synthesis of the discussion from the floor and, in a foreword to the published volume, MacLeod will give his views on the implications of the symposium for future research.

Chemical Engineers

The 41st national meeting of the American Institute of Chemical Engineers will be held at the Hotel St. Paul, St. Paul, Minn., 27–30 September. Some 2000 participants are expected.

General chairman is W. M. Poda, Economics Laboratory, St. Paul. The technical program is being arranged by A. J. Madden, Jr., of the Institute of Technology, University of Minnesota. The program will include sessions on research, new product development, chemical warfare, safety, missile construction materials, and chemical economics as a unit process. A student program is being prepared by W. E. Ranz and H. S. Isbin of the University of Minnesota.

Forthcoming Events

September

14–18. American Dental Assoc., New York, N.Y. (H. Hillenbrand, 222 E. Superior St., Chicago 11, Ill.)

14–19. High Energy Accelerators and Instrumentation, intern. conf., Geneva, Switzerland. (Conference Secretariat, CERN, Geneva 23.)

14–19. Treatment of Waste Waters, symp., Newcastle upon Tyne, England. (Wastes Symposium, Public Health Engineering Section, Dept. of Civil Engineering, King's College, Newcastle upon Tyne, 2.)

18–21. European League against Rheumatism, cong., Istanbul, Turkey. (H. Kocas, Medical School, Ankara, Turkey.)

18–25. International Council for Philosophy and Humanistic Studies (5th meeting of the general assembly), Ann Arbor, Mich. (ICPHS, 19, avenue Kleber, Paris 16e, France.)

19–22. Planning of Science, intern. symp., Prague, Czechoslovakia. (Secre-

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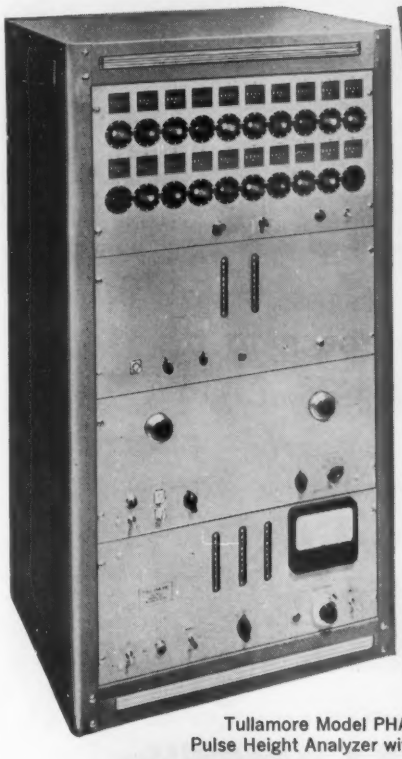

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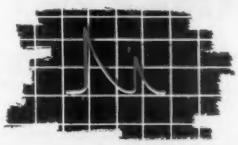

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tary, Intern. Symp. on Planning of Science, Gorkho Manesti 23, Prague 3.)

19–26. American College of Gastroenterology, Los Angeles, Calif. (D. Weiss, 33 W. 60 St., New York 23.)

20–25. Biological Standardization, 5th intern., Lyon, France. (C. Merieux, 17, rue Bourgelat, Lyon.)

21–24. International Dental Federation, 47th annual, New York, N.Y. (IDF, 35 Devonshire Pl., London W.1.)

21–25. Instrument-Automation Conf., 14th annual, Chicago, Ill. (R. T. Devore, Instrument Soc. of America, 313 Sixth Ave., Pittsburgh, Pa.)

21–26. Mother-Infant Interaction and Its Relation to Mental Health, Ciba Foundation symp. (by invitation), London, England. (G. E. W. Wolstenholme, Ciba Foundation, 41 Portland Pl., London, W.1.)

21–28. Biology of Sardines (FAO world meeting), Rome, Italy. (FAO, Viale delle Terme di Caracalla, Rome.)

21–3. Permanent Intern. Assoc. of Road Congresses, quadrennial congress, Rio de Janeiro, Brazil. (PIARC, 43, Avenue du President Wilson, Paris 16e, France.)

22–24. Some Aspects of Magnetism, conf., Sheffield, England. (Conference Secretary, Inst. of Physics, 47 Belgrave Sq., London, S.W.1, England.)

22–25. American Roentgen Ray Soc., Cincinnati, Ohio. (C. A. Good, Mayo Clinic, Rochester, Minn.)

22–26. Cancer Cytology, intern. conf., Madrid, Spain. (Miss E. L. Hughes, 3007 Salzedo, Coral Gables, Fla.)

23. Association for the Advancement of Psychoanalysis, New York, N.Y. (New York Acad. of Medicine, 2 E. 103 St., New York.)

23–2. International Film Cong., 13th, London and Oxford, England. (Intern. Scientific Film Assoc., 3 Belgrave Sq., London S.W.1.)

24–25. Solid Propellants Conf. (American Rocket Soc.), Princeton, N.J. (A. F. Denham, ARS, 925 Book Bldg., Detroit 26, Mich.)

24–26. American Assoc. of Medical Clinics, Chicago, Ill. (E. P. Jordan, Box 58, Charlottesville, Va.)

24–26. American Assoc. for the Surgery of Trauma, Bretton Woods, N.H. (W. T. Fitts, Jr., 3400 Spruce St., Philadelphia 4, Pa.)

24–26. Central Assoc. of Obstetricians and Gynecologists, Chicago, Ill. (E. J. DeCosta, 104 S. Michigan Ave., Chicago 3.)

27–30. American Inst. of Chemical Engineers, natl., St. Paul, Minn. (F. J. Van Antwerpen, AICE, 25 W. 45 St., New York 36.)

28–30. American Oil Chemists' Soc., fall, Los Angeles, Calif. (Mrs. L. R. Hawkins, AOCS, 35 E. Wacker Drive, Chicago 1, Ill.)

28–30. Telemetering, natl. symp., San Francisco, Calif. (G. L. Larse, Lockheed Aircraft Corp., Missile Systems Div., Sunnyvale, Calif.)

28–1. Recent Developments in Research Methods and Instrumentation, 9th annual symp. and exhibit, NIH, Bethesda, Md. (J. B. Davis, National Institutes of Health, Public Health Service, Bethesda 14.)

28–2. American College of Surgeons, 45th clinical cong., Atlantic City, N.J. (R. M. Cunningham, Jr., ACS, 40 E. Erie St., Chicago 11, Ill.)

30–1. Industrial Electronics, 8th annual symp., Pittsburgh, Pa. (R. H. Delgado, 954 Brentview Dr., Pittsburgh 36.)

30–1. Mississippi Valley Medical Soc., St. Louis, Mo. (H. Swanberg, 510 Maine St., Quincy, Ill.)

October

1–4. American Soc. of Industrial Designers, Asheville, N.C. (Mrs. R. R. Larisch, ASID, 15 E. 48 St., New York 17.)

1–4. Electrochemical Thermodynamics and Kinetics, annual intern., Vienna, Austria. (M. P. Van Rysselberghe, CITE for the U.S., Dept. of Chemistry and Chemical Engineering, Stanford Univ., Stanford, Calif.)

4–7. American Inst. of Mining, Metallurgical and Petroleum Engineers, fall, Dallas, Tex. (E. O. Kirkendall, AIMMPE, 29 W. 39 St., New York 18.)

4–9. Society of Motion Picture and Television Engineers, semi-annual conv., New York, N.Y. (C. S. Stodter, SMPTE, 55 W. 42 St., New York, 36.)

5–7. Aeronautical Communications, 5th symp., Utica, N.Y. (L. G. Cumming, Inst. of Radio Engineers, 1 E. 79 St., New York 21.)

5–7. Chemical Engineers, annual, Essen, Germany. (Dr. Miessner, VDI-Fachgruppe, Verfahrenstechnik, Rheingauallee 25, Frankfurt-am-Main, Germany.)

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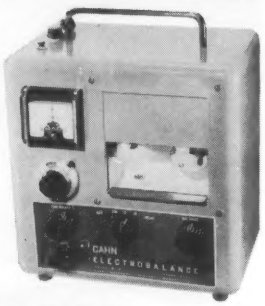

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5–7. National Assoc. of Corrosion Engineers, Northeast regional, Baltimore, Md. (T. J. Hull, NACE, 1061 M & M Bldg., Houston, Tex.)

5–8. American Acad. of Pediatrics, Chicago, Ill. (E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill.)

5–9. American Soc. of Anesthesiologists, Bal Harbour, Fla. (J. W. Andes, 188 W. Randolph St., Room 1101, Chicago, Ill.)

5–9. Audio Engineering Soc., 11th annual, New York, N.Y. (AES, P.O. Box 12, Old Chelsea Station, New York 11.)

5–10. Society of Automotive Engineers, aeronautical meeting and aircraft manufacturing forum, Los Angeles, Calif. (R. W. Crory, Meetings Operation Dept., SAE, 485 Lexington Ave., New York 17.)

5–16. Institute of the Aeronautical Sciences, biennial Anglo-American conf., New York, N.Y. (R. R. Dexter, IAS, 2 E. 64 St., New York 21.)

6–8. Aeronautical/Astronautical Problems of High Speed Flight, Stanford, Calif. (E. Haynes, Deputy Director, Aero Sciences Directorate, Air Force Office of Scientific Research, Washington 25.)

6–9. High Temperature Technology, intern. symp., Asilomar, Calif. (Public Relations Office, Stanford Research Inst., Menlo Park, Calif.)

7–8. Advanced Propulsion, 2nd symp. (classified), Boston, Mass. (Lt. Col. P. Atkinson, Propulsion Div., Air Force Office of Scientific Research, Washington 25.)

7–9. Vacuum Technology, symp., Philadelphia, Pa. (American Vacuum Soc., Box 1282, Boston, Mass.)

7–11. International Conv. on Nutrition and Vital Substances, 5th, Konstanz-Zurich, Switzerland. (Secretary General, Benmeroderstrasse 61, Hannover-Kirchrode, Germany.)

8–10. American Assoc. of Textile Chemists and Colorists, natl. conv., Washington, D.C. (G. P. Paine, AATCC, P.O. Box 28, Lowell, Mass.)

8–10. American Ceramic Soc., Bedford, Pa. (F. P. Reid, ACS, 4055 N. High St., Columbus 14, Ohio.)

8–10. American Soc. of Tool Engineers, semi-annual, St. Louis, Mo. (H. E. Conrad, ASTE, 10700 Puritan Ave., Detroit 38, Mich.)

8–10. Biology of Pyelonephritis, intern. symp., Detroit, Mich. (E. L. Quinn, Henry Ford Hospital, W. Grand Blvd. at Hamilton, Detroit 2.)

8–10. Optical Soc. of America, annual, Ottawa, Canada. (S. S. Ballard, Dept. of Physics, Univ. of Florida, Gainesville.)

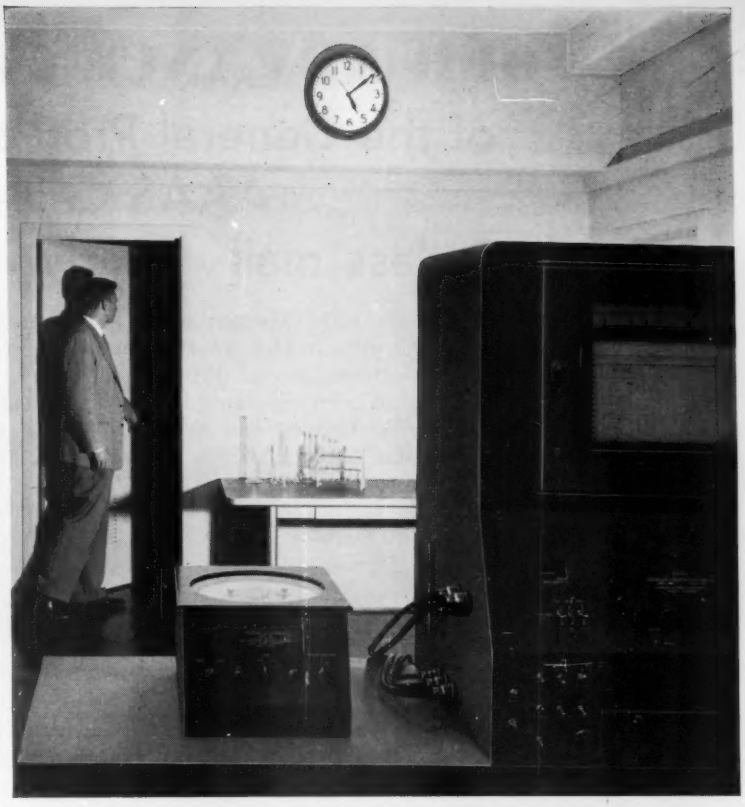
9–13. American Soc. of Civil Engineers, Los Angeles, Calif. (E. S. Kirkpatrick, ASCE, 33 W. 39 St., New York 18.)

11–16. American Acad. of Ophthalmology and Otolaryngology, Chicago, Ill. (W. L. Benedict, 15 Second St., SW, Rochester, Minn.)

11–16. American Inst. of Electrical Engineers, fall general, Chicago, Ill. (N. S. Hibshman, AIEA, 33 W. 39 St., New York 18.)

11–16. American Soc. for Testing Materials, Pacific area natl., San Francisco, Calif. (R. J. Painter, ASTM, 1916 Race St., Philadelphia 3, Pa.)

12–14. Clay Conf., 8th natl., Norman, Okla. (C. G. Dodd, Eighth Natl. Clay



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The General Program of the 126th Meeting of the AAAS in Chicago, 26–31 Dec., 1959, will be available to you within the first week in December—whether you can attend the Meeting or not.

Effective this year, the former General Program-Directory, which had become an unwieldy book of more than 400 pages, has been separated into **two** publications, namely:

a) The Directory of AAAS Officers and Activities, 96 pp., already published; and

b) The General Program of the Annual Meeting, c. 200 pp., which will appear early in December.

Both of these, sold at cost, may be purchased separately—in advance (see coupon below), or at the meeting. Some of their *respective* contents are:

The General Program

1. The two-session general symposium, "Moving Frontiers of Science IV," arranged by the Committee on AAAS Meetings.
2. Programs of the 18 AAAS sections (symposia and contributed papers).
3. Programs of the more than 70 participating societies.
4. Sessions of the Conference on Scientific Communication, Conference on Scientific Manpower, and the Academy Conference.
5. The Special Sessions: AAAS Address and Reception, National Geographic Society, Phi Beta Kappa, Sigma Xi, RESA, Tau Beta Pi Association.
6. Details of the Morrison Hotel—center of the Meeting—and of the other session sites.
7. Titles of the latest foreign and domestic scientific films to be shown in the AAAS Science Theatre.
8. Exhibitors in the 1959 Annual Exposition of Science and Industry and descriptions of their exhibits.

The Directory

1. AAAS officers, staff, committees for 1959.
2. Section committees and other AAAS Council members.
3. The 285 affiliated organizations.
4. Historical sketch and organization of the Association.
5. Complete roll of AAAS presidents and their fields.
6. Publications of the Association, including all symposium volumes.
7. AAAS Awards—including all past winners.
8. Future Meetings of the AAAS through 1963.
9. New and current activities of the AAAS.
10. Constitution and Bylaws.

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Conf., University of Oklahoma, Norman.)

12–14. Electronics Conf., 15th annual natl., Chicago, Ill. (NEC, 228 N. La Salle St., Chicago 1, Ill.)

12–16. Macromolecules, intern, symp. (IUPAP), Wiesbaden, Germany. (W. Mauss, Intern. Symp. on Macromolecules, c/o Kalle & Co., Rheingaustrasse 25, Wiesbaden-Biebrich, Germany.)

12–19. Venereal Diseases, intern. cong. (by invitation), London, England. (G. E. W. Wolstenholme, Ciba Foundation, 41 Portland Pl., London, W.1, England.)

13–17. International Union against the Venereal Diseases and the Treponematoses, London, England. (Institut Alfred Fournier, 25, Boulevard Saint-Jacques, Paris 14e, France.)

14–16. Parenteral Drug Assoc., annual conv., New York, N.Y. (H. E. Boyden, Parenteral Drug Assoc., 130 E. 59 St., New York 22.)

14–17. American College of Chest Physicians, 25th, Albuquerque, N.M. (M. Kornfeld, 112 E. Chestnut St., Chicago 11, Ill.)

15–16. American Ceramic Soc., Glass Div., Wernersville, Pa. (F. P. Reid, ACS, 4055 N. High St., Columbus 14, Ohio.)

15–17. Academy of Psychosomatic Medicine, Cleveland, Ohio. (B. B. Moss, Suite 1035, 55 E. Washington St., Chicago 2.)

15–17. National Soc. of Professional Engineers, fall meeting, Seattle, Wash. (P. H. Robbins, NSPE, 309 Bancroft Bldg., Univ. of Nebraska, Lincoln.)

16–17. Association of Midwest College Biology Teachers, conf., Notre Dame, Ind. (G. R. Bernard, Dept. of Biology, Univ. of Notre Dame, Notre Dame, Ind.)

17–18. American Acad. of Psychotherapists, 4th annual conf., New York, N.Y. (AAP, 30 Fifth Ave., New York 11.)

17–25. Plastics Industry, intern. fair, Düsseldorf, Germany. (Nordwestdeutsche Ausstellungs Gesellschaft (NOWEA), Ehrenhof 4, Düsseldorf.)

18–22. Electrochemical Soc., Columbus, Ohio. (R. K. Shannon, ES Inc., 216 W. 102 St., New York 25.)

18–23. American School Health Assoc., Atlantic City, N.J. (A. O. DeWeese, 515 E. Main St., Kent, Ohio.)

18–23. American Soc. of Plastic and Reconstructive Surgery, Miami Beach, Fla. (T. R. Broadbent, 508 E. South Temple, Salt Lake City, Utah.)

19–21. High Polymer, 9th Canadian, Toronto, Ontario, Canada. (K. E. Russell, Dept. of Chemistry, Queen's Univ., Kingston, Ontario.)

19–22. Semiconductor Symp. (Electrochemical Soc.), Columbus, Ohio. (A. C. Beer, Battelle Memorial Inst., 505 King Ave., Columbus 1, Ohio.)

19–23. American Public Health Assoc., 87th annual, Atlantic City, N.J. (B. F. Mattison, 1790 Broadway, New York 19, N.Y.)

19–23. American Soc. of Civil Engineers, annual conv., Washington, D.C. (W. H. Wisley, ASCE, 33 W. 39 St., New York 18.)

19–31. International Cong. of Therapeutics, Strasbourg, France. (Prof. Fontaine, Dayen de la Faulte de Strasbourg, France.)

19–31. Pan American Medical Assoc., 10th conf., Mexico, D.F., Mexico. (J. Eller, PAMCA, 745 Fifth Ave., New York 22.)

20–22. Standards, 10th natl. conf., Detroit, Mich. (K. G. Ellsworth, American Standards Assoc., 70 E. 45 St., New York 17.)

20–23. Clean Air, intern. conf., London, England. (National Soc. for Clean Air, Palace Chambers, Bridge St. London, S.W.1, England.)

22–24. Acoustical Soc. of America, fall meeting, Cleveland, Ohio. (W. Waterfall, ASA, 335 E. 45 St., New York 17.)

22–24. American Documentation Inst., annual, Bethlehem, Pa. (R. S. Taylor, Lehigh Univ., Bethlehem, Pa.)

22–25. British Medical Assoc., annual clinical, Norwich, England. (W. Hedgcock, BMA House, Tavistock Sq., London, W.C.1, England.)

23–24. Canadian Soc. for the Study of Fertility, Montreal, Canada. (J. F. Campbell, 238 Queen's Ave., London, Ont., Canada.)

23–25. American College of Cardiology, 8th annual, Philadelphia, Pa. (P. Reichert, ACC, Empire State Bldg., New York 1.)

23–27. American Heart Assoc., annual, Philadelphia, Pa. (W. F. McGlone, AHA, 44 E. 23 St., New York 10.)

24–29. Darwin Centennial, intern. cele-

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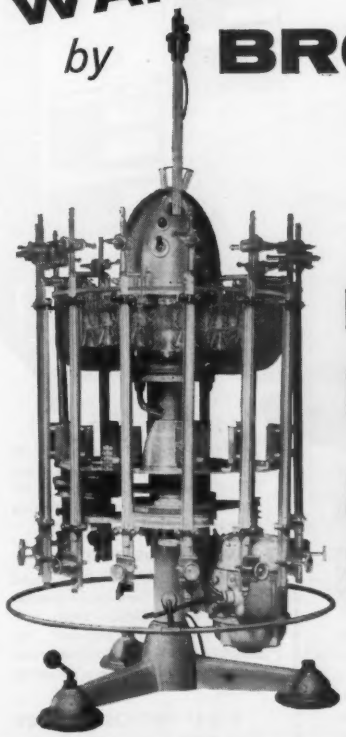

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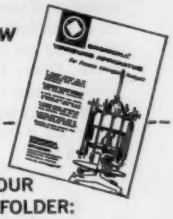

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PLEASE SEND YOUR NEW WARBURG FOLDER:
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bration, Chicago, Ill. (Office of Public Relations, Univ. of Chicago, Ill.)

24–29. First All-India Cong. of Zoology, Jabalpur. (B. S. Chauhan, Zoological Survey of India, 34 Chittaranjan Ave., Calcutta 12.)

27–27. Griseofulvin and Dermatomycoses, intern. symp., Miami, Fla. (H. Blank, Dept. of Dermatology, Univ. of Miami School of Medicine, Miami 36.)

26–28. Aeronautical and Navigation Electronics, IRE conf., Baltimore, Md. (L. G. Cumming, IRE, 1 E. 79 St., New York 21.)

26–28. Analytical Chemistry in Nuclear Reactor Technology, 3rd conf., Gatlinburg, Tenn. (C. D. Susano, Oak Ridge Natl. Lab., P.O. Box Y, Oak Ridge, Tenn.)

26–28. Gas Lubricated Bearings, 1st intern. symp., Washington, D.C. (S. W. Doroff, Power Branch, Office of Naval Research, Washington 25.)

26–28. National Rehabilitation Assoc., Boston, Mass. (E. D. Callahan, 14 Court Square, Boston 8.)

26–28. Society of Automotive Engineers, natl. transportation meeting, Chicago, Ill. (R. W. Crory, SAE, 485 Lexington Ave., New York 17.)

26–30. Society of Photographic Scientists and Engineers, natl. conf., Chicago, Ill. (SPSE, Box 1609, Main Post Office, Washington, D.C.)

NEW

Tudor Modular Cabinets

BY

LAB-TEK

Modules "stack-file" in one compact unit.

TISSUE-TEK 1000

Simplified, compact storing and filing for Tissue-Tek embedding rings. Deluxe metal cabinet has 6 hi-impact plastic drawers to provide storage for 1000 rings.

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2000 standard 3" x 1" slides stored in polyurethane-lined compartments. Drawer liners cushion slides and assist convenient "pop-out" removal. Vented design allows complete drying of cover slip mounting media.

2"x2" PHOTOSLIDE 3000

Stores 3000 standard 2"x2" photoslides. Six plastic drawers in each Tudor Module.

Safe, Accurate and Convenient

Tudor Modular cabinets — precision engineered for laboratory filing and storage. Durably constructed of heavy gauge steel with reinforced corners, double-wall panels and hi-impact plastic drawers. Stacked in a vertical column, they use less than 2 sq. ft. of floor space. Doors have hideway design which permits complete access to plastic filing drawers. Smooth rolling castered base permits easy cabinet movement.

For safe filing and compact storage, use versatile Tudor Modular Cabinets by Lab-Tek!

LAB TEK PLASTICS CO.

Contact your Lab-Tek Dealer or write

LAB-TEK PLASTICS CO.

39 East Burlington Ave.
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New Products

The information reported here is obtained from manufacturers and from other sources considered to be reliable, and it reflects the claims of the manufacturer or other source. Neither Science *nor the writer assumes responsibility for the accuracy of the information. A coupon for use in making inquiries concerning the items listed appears on page 470.*

■ VECTOR IMPEDANCE LOCUS PLOTTER is a portable laboratory instrument designed to measure continuously and plot automatically and simultaneously the rectangular components, resistance and reactance, of the equivalent complex impedance of any passive electrical element. (Chesapeake Instrument Corp., Dept. 1)

■ RANDOM NOISE SOURCE provides a choice of balanced or unbalanced calibrated output, each with several impedances. Noise figure, defined as the ratio of actual noise power to ideal-system noise power, may be read directly from a meter. Frequency range is 5 to 220 Mcy/sec. Noise-figure range is 0 to 16 db at nominal 50-ohm impedance and 0 to 23.8 db at 300 ohm. The indicating meter is calibrated logarithmically in decibels for noise figure and linearly in milliamperes d-c. (Kay Electric Co., Dept. 2)

■ COMPACTOR uses kneading action to prepare samples of bituminous mixes, asphaltic concrete, soils, and similar materials. Compaction pressure, time of dwell, and rate of compaction are adjustable. Two molds (4 and 6 in. in diameter) are provided. A heated-foot assembly is available, as an accessory. Manual or automatic electrohydraulic operation is provided. (Soiltest, Dept. 3)

■ COMPARISON BRIDGE measures resistance, capacitance, and inductance at 60 cy/sec. Resistance range is 3 ohm to 5 megohm; capacitance 500 pf to 1000 μf; inductance 3 mh to 10,000 hy. Five meter ranges indicate full-scale differences from 1 to 25 percent. Accuracy on range 1 is ±0.1 percent. A switch that may be foot-operated protects the meter circuit during insertion or removal of components. (Metronix Inc., Dept. 4)

■ RESONANT REED RELAY responds by contact closure, for a fraction of each cycle, to signals of proper frequency. A typical relay provides 32 channels from 30 to 1000 cy/sec with bandwidths less than 1.5 percent and sensitivity of 1.5 mw. Frequency variation with temperature is less than ±0.5 percent from −60° to +150°F. The device is resistant to vibration up to 10 *g* in the plane of reed motion and to 20 *g* in the other axes for vibration frequencies between 20 and 800 cy/sec. Size is ½ in.² by 1⅛ in. (Wurlitzer, Dept. 8)

■ FUNCTION GENERATOR contains up to ten curves, each printed on a thin plastic sheet, all of which are pressed together into a single laminated sheet approximately 3/64 in. thick. The laminated sheet is made to fit the manufacturer's recorder-curve follower. A cable-connected switch unit permits selection of individual curves to be followed. Any desired function can be printed. An initial model contains ten common functions. (F. L. Moseley, Dept. 6)

■ X-Y RECORDER consists of an 11-by-17-in. plotter with separate input modules for general-purpose, computer, low-level differential, time-base, curve-following, and other specialized functions. Function modules are remotely operated. Internal calibration, accurate to ± 0.05 percent, is provided by a Zener diode reference. Record paper is held down by vacuum. (Electro Instruments, Dept. 5)

■ POWER SUPPLY for cathode-ray tubes provides all power required for high-intensity cathode-ray tubes with pre- and post-acceleration, including focus and intensity controls and coupling condensers, in a space less than 2.5 by 4 by 5.5 in. The unit can be operated at altitudes up to more than 70,000 ft without pressurization. Input is 115 v, 380 to 1500 cy/sec; outputs are 6.3 v at 1 amp, 2.5 kv at 100 μa, and – 2.5 kv up to 500 μa. Ripple value in a typical circuit is said to be less than 1 percent. (Avionics Research Products, Dept. 13)

■ INTEGRATING MANOMETER reads average of pressures indicated by 2 to 49 manometers. Averaging is accomplished by using precision-bore tubing and providing cross-manifold, cross-reservoir, and guillotine-type values for individual tubes. The unit may be used without modification as a standard multibank manometer. (Dynametrics, Dept. 10)

■ ESTERS are described in 48-page booklet which outlines the properties and applications of 26 esters. Basic reference data are provided by 27 graphs and tables which show evaporation rates, viscosities of solutions, dilution ratios, specific gravities, constant boiling mixtures, and other properties. A detailed bibliography is included (Union Carbide Chemicals, Dept. 15)

■ ENVIRONMENTAL TEST CHAMBER is designed to fit into a standard 19-in. relay rack. Chamber volume is 1.5 ft^3. The unit is furnished with indicating controller, forced-air circulator, electric heating, and direct refrigeration; it is available mounted or separate. (Conrad, Dept. 14)

JOSHUA STERN
National Bureau of Standards, Washington, D.C.

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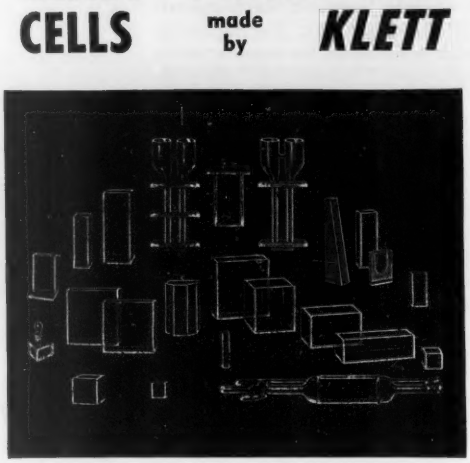

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Replies to blind ads should be addressed as follows:

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POSITIONS WANTED

Medical Mycologist. Ph.D. For research and teaching. Broad experience with fungi, tubercle bacilli, actinomycetes, transduction, genetics. Box 193, SCIENCE. 8/14, 21

Medical Abstracting or Writing. Experience ethical pharmaceutical house. Box 202, SCIENCE. X

Microbiologist, Ph.D. Desires teaching or research position. Box 198, SCIENCE. X

POSITIONS WANTED

Neuroanatomist-Neurophysiologist, Ph.D. Zoology and medical school teaching; Phi Kappa Psi, Alpha Kappa Kappa, Sigma Xi. Age 33; 14 publications. Curriculum vitae write Box 200, SCIENCE. 8/28; 9/4, 11, 18, 25

Pharmacologist-Psychologist, more than 10 years' experience in industrial pharmacology; recent M.A. in psychology. Desires industrial personnel or administration. Prefer southern location. Box 195, SCIENCE. X

Plant Physiologist, Botanist, Ph.D. Desires research opportunity biochemical, experimental morphogenesis; or curatorial position economic botany—noxious, cryptogamic plants. Editorial work considered. Box 201, SCIENCE. X

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ELECTRONIC ENGINEER OR PHYSICIST

Manufacturer of synthetic fibers with subsidiary interests in the field of electronic components is expanding its research efforts in electronics and has an opening for an electronic engineer or a physicist with strong theoretical background and experience in electronics to assist in the design of experiments for achieving specified research goals in the field of dielectric materials. Will be responsible for testing the physical and electrical properties of specialty insulators for micro-wave systems.

Pleasant working and living location near Asheville, N.C. Excellent benefits; 5-day work week; moving expenses. Send complete résumé, including salary requirements, to Employment Manager, Enka, N.C.

AMERICAN ENKA CORPORATION

POSITIONS OPEN

(a) Bacteriologist; Ph.D., equivalent, experienced medical bacteriology, able supervise this section, work of five employees; 450-bed general teaching hospital; to $9000; eastern metropolitan area. **(b) Biochemist;** excellent opportunity for qualified Ph.D. to supervise clinical section, teach technologists, establish new tests; some research opportunity; three new laboratories under construction in 400-bed general hospital; to $12,000; Midwest. **(c) Chemist;** B.S., M.S., qualified in latest procedures; well-equipped, busy county public health laboratory; minimum $6500; New York. **(d) Bacteriologist;** M.S. to head busy department in active laboratory, 400-bed hospital; some teaching; to $7200; midwestern college city 50,000. **(e) Biochemist;** Ph.D. experienced in coagulation, train in-plant visitors, keep abreast of competitive products, deliver coagulation seminars; about $10,000; eastern pharmaceutical concern. Woodward Medical Bureau, Ann Woodward, Director, 185 North Wabash, Chicago. X

Biological Production. Opportunity for top production man, either D.V.M. or Ph.D., biological production with an ethical veterinary supply company. Requirements include biological production experience, administrative and executive potential, and ability to direct people. Opportunity for growth. Salary commensurate with training and experience. Other employee benefits. Box 196, SCIENCE. 8/28; 9/4

College Textbook Representative

Creative opening in Northeast or Midwest for expanding department of leading technical publisher. Young man with publishing and/or science or engineering background required. Replies confidential. Send résumé.

Box 199, SCIENCE

POSITIONS OPEN

LITERATURE SCIENTISTS

To evaluate, abstract, and code scientific information for mechanized literature retrieval system. Training in biological or medical sciences. Writing and foreign-language abilities. Reply to

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Pharmacologist, M.D. or Ph.D. to organize and direct new laboratory in growing pharmaceutical operations of N.Y.S.E. listed company. Candidate should have broad interest, practical approach and working familiarity with evaluation procedures in diverse fields of drug action. Excellent opportunity for well-trained young man for key position. Submit résumé, discussion of interest, photo, and salary requirements. Confidence will be fully respected. Box 190, SCIENCE. 8/21

Ph.D., Pharmacologist. With interest in drug evaluation and pharmacodynamics for position of senior pharmacologist with expanding research department of midwestern pharmaceutical company. Some industrial experience preferred. Send vita and salary record to Box 178, SCIENCE. 7/31; 8/7, 14

Research Associateship available in synthetic organic chemistry with emphasis on heterocyclic nitrogen and oxygen compounds. Salary dependent upon qualifications. Charles H. Jarboe, Department of Pharmacology, University of Louisville, School of Medicine, Louisville 2, Ky. X

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SENIOR SCIENTIST

Research openings in expanding pharmaceutical company located in non-metropolitan central New York State community:

Pharmacologist, Ph.D., Cardiovascular
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Bacteriologist, Ph.D., Research and Development
Information Scientist, Ph.D., Biological Sciences

forward your resume to
Professional Employment Manager
EATON LABORATORIES DIVISION
THE NORWICH PHARMACAL CO.
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POSITIONS OPEN

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Wyeth Laboratories Inc. has need for the services in the Philadelphia area of a scientist, Ph.D. in mycology or allied science, with heavy experience in fermentation processes.

This research man should also have administrative ability—he will supervise a microbiological group consisting of both degree and non-degree people.

Salary commensurate with ability and experience. Please send complete résumé, including present salary, to:

Personnel Department
Wyeth Laboratories Inc.
611 E. Nield Street
West Chester, Pa.

All replies held in confidence.

POSITIONS OPEN

Physiologist or Biochemist. Research institution with possible academic affiliation; good facilities for independent research. Salary dependent on qualifications and experience; Philadelphia. Box 203, SCIENCE. 8/28

FELLOWSHIPS

Microbiologist-Biochemist. Recent or prospective Ph.D. Research fellowship for biochemical studies on autotrophic bacteria. Active biology department. Box 187, SCIENCE. 8/7, 14, 21

Predoctoral and Postdoctoral Fellowships for geneticists and microbiologists in field of experimental animal caries. Stipend: predoctoral, $1800 first year; $200 increase each additional year; $500 allowance for each dependent. Postdoctoral, $4500 first year, $500 increase each additional year, $500 allowance for each dependent. Write to Dr. H. R. Hunt, Department of Zoology, Michigan State University, East Lansing, Michigan. X

USE THIS EASY SELF-MAILER to obtain further information

21 August 1959

Readers' Service

Information Requisition

It's simple: Mark—Clip—Fold—Mail—No stamp required

This coupon is for your convenience—to facilitate your requests for further information about advertised products and items in New Products. This coupon is good for 3 months only.

From:

Name ..... **Position** .....

Company .....

Street .....

City ..... **Zone** ..... **State** .....
(Please print or type)

Mark, clip coupon—FOLD HERE along this line—mail

Postage Will be Paid by Addressee

No Postage Stamp Necessary If Mailed in the United States

BUSINESS REPLY MAIL
First Class Permit #12711 New York, N.Y.

Readers' Service

To: SCIENCE MAGAZINE
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11 West 42 Street
New York 36, New York

Fasten Here Only
Staple, Tape, Glue

The Market Place

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Editor: Reidar F. Sognnaes

Price $6.75; AAAS Members' prepaid order price $5.75

246 pp. 49 illus., index, clothbound. 1955

This is the first monograph specifically devoted to data from the experimental production and prevention of tooth decay in laboratory animals. Twenty distinguished investigators, representing dentistry and allied basic sciences, report and review their researches. Unusually well organized, the book represents a coherent sequence, and is skillfully summarized by the editor in a final chapter, followed by very detailed subject and author indexes.

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P.O. Box 1375 Wasco, California

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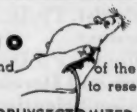
albino rats*



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* CHARLES RIVER S D (Sprague-Dawley descendants)
* CHARLES RIVER W (Wistar descendants)

THE CHARLES RIVER BREEDING LABS
Dept. B 1093 Beacon St. Brookline 46, Mass.

21 August 1959

Readers' Service

Information Requisition

Use this easy self-mailer to obtain further information about items or literature from the New Products section as well as advertised products.

NEW PRODUCTS

Circle below desired number corresponding to:

1 2 3 4 5 6 8 10
13 14 15

ADVERTISERS IN THIS ISSUE

In the below list, check page number of advertiser from whom you would like more information. If more than one item appears in ad, letters **A, B, C** are used to indicate particular items available in order of appearance in advertisement. Where more than one ad appears on page, **U** indicates upper ad, **L** lower ad, **I** inside ad, **M** middle ad, and **O** outside ad. The covers are designated by **IFC** (inside front cover), **IBC** (inside back cover), and **OBC** (outside back cover). Advertisements in Personnel Placement are not keyed; only fractional pages (one-sixth or larger) in the Market Place are keyed. A multiplicity of items is indicated by *. Readers are requested to specify on this coupon the particular item in which they are interested; otherwise, the request cannot be processed.

☐ IFC	☐ 411*	☐ 412*	☐ 413	☐ 414
☐ 415	☐ 416	☐ 420	☐ 457	☐ 458,UO
☐ 458,UI	☐ 458,LO	☐ 458,LI	☐ 459	☐ 460
☐ 461	☐ 462	☐ 463	☐ 465	☐ 466
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The latest word in automatically-controlled, refrigerated centrifuges

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BASIC UNIT INCLUDES STANDARD 8 x 50 ml SUPERSPEED ROTOR

Write for more information about this, the Superspeed Automatic Refrigerated Centrifuge that researchers everywhere have been asking for: Bulletin **SC-8RC-2.**

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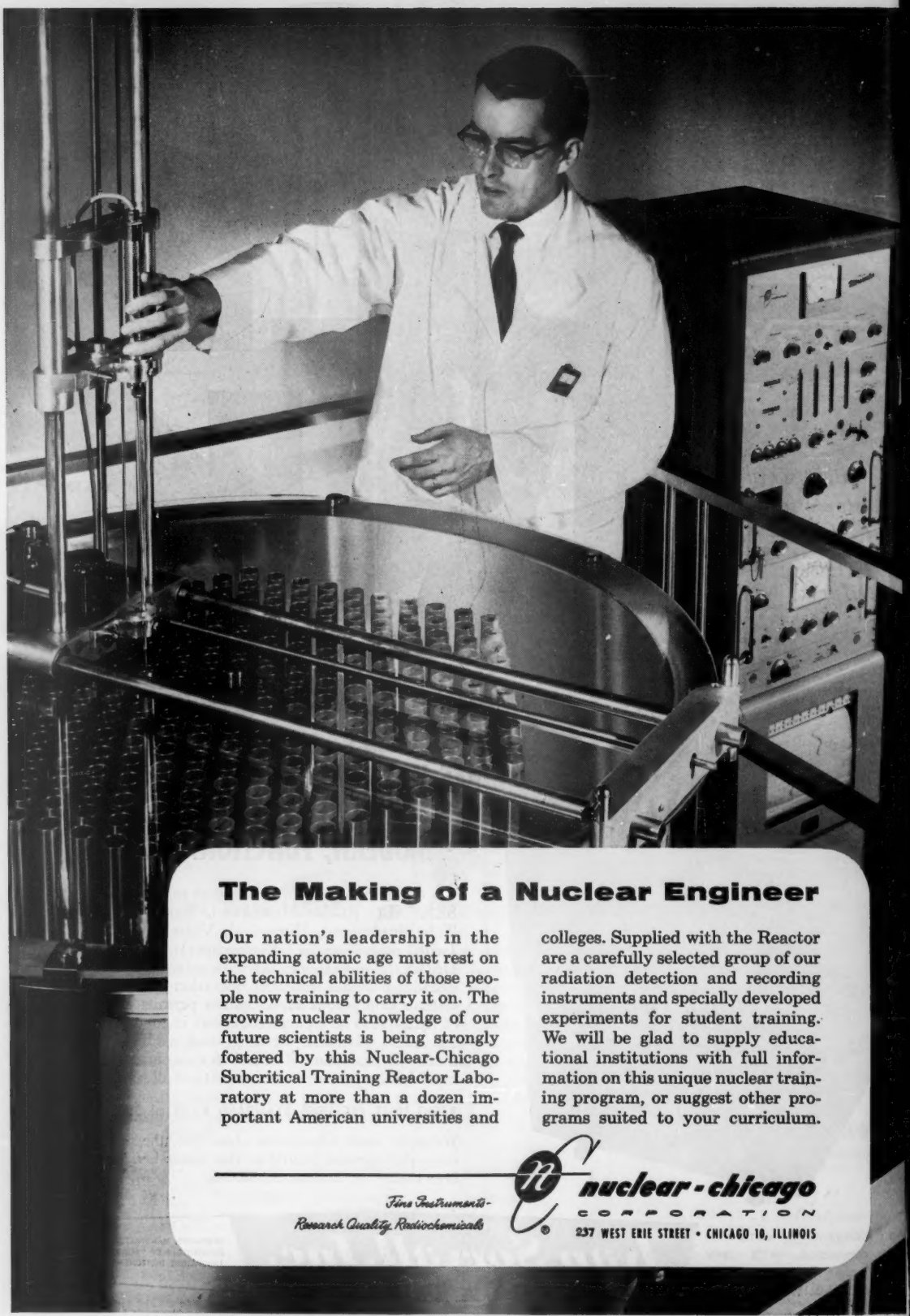

The Making of a Nuclear Engineer

Our nation's leadership in the expanding atomic age must rest on the technical abilities of those people now training to carry it on. The growing nuclear knowledge of our future scientists is being strongly fostered by this Nuclear-Chicago Subcritical Training Reactor Laboratory at more than a dozen important American universities and colleges. Supplied with the Reactor are a carefully selected group of our radiation detection and recording instruments and specially developed experiments for student training. We will be glad to supply educational institutions with full information on this unique nuclear training program, or suggest other programs suited to your curriculum.

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